Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1. Questionnaire questions

Phenotype	Question asked
Collodion-membrane	Were you born with a 'parchment' or 'cellophane' (collodion) membrane covering your skin?
Skin pain	Do you have pain in your skin?
Pruritus	Does your skin itch?
Skin odor	Does your skin have an odor?
Skin infections	Have you had problems with infections of your skin?
Hypohydrosis	Do you perspire normally—not at all, less than most people, more than most people
Hearing problems	Did you now or at one time have hearing or other ear problems?
Eye problems	Does the light hurt your eyes? Can you fully close your eyes when sleeping? Do you now or did you at one time have other eye problems (e.g. cataracts, photophobia, ectropion, corneal erosions, scarring, impaired vision, glaucoma, blindness, etc)?
Alopecia	Do you have any hair loss?

eTable 2a. Kindreds with recessive inheritance (n=629)

GENE	TOTAL KINDREDS	COMPOUND HETEROZYGOUS	HOMOZYGOUS
TGM1	169	113	56
ABCA12	66	57	9
ALOX12B	63	47	16
NIPAL4	56	14	42
****STS***	47	N/A	N/A
FLG	46	33	13
ALOXE3	40	22	18
SPINK5	30	20	10
PNPLA1	29	16	13
CYP4F22	17	7	10
ABHD5	9	3	6
KDSR	6	6	0
ALDH3A2	6	2	4
CERS3	5	2	3
SDR9C7	6	3	3
CDSN	4	1	3
****MBTPS2***	4	N/A	N/A
AP1B1	3	1	2
CSTA	3	1	2
SLC27A4	3	2	1
SNAP29	2	0	2
ST14	4	0	4
TGM5	3	3	0
CAST	1	0	1
CLDN1	1	0	1
ERCC2	1	1	0
KANK2	1	0	1
LSS	1	1	0
RSPO1	1	0	1
SERPINB7	1	1	0
PERP	1	0	1
TOTAL	**629**	**356**	**222**

**indicates X-linked inheritance*

eTable 2b. Kindreds with dominant inheritance (n=240)

GENE	TOTAL KINDREDS
KRT10	94
KRT1	31
ATP2C1	18
KRT2	17
GJB2	14
ATP2A2	15
GJA1	8
DSP	7
DSG1	5
GJB4	4
GJB3	3
LOR	4
NSDHL	3
DSC2	2
EBP	2
POGLUT1	2
RHBDF2	2
TRPV3	2
ASPRV1	1
CARD14	2
ELOVL1	1
GJB6	1
KRT14	1
SREBF1	1
TOTAL	**240**

eTable 3. Novel mutations (n=266)

Gene	Nucleotide change	Amino acid change	Race/ethnicity
ABCA12	c.2827G>C	p.A943P	Black
ABCA12	c.7536C>A	p.Y2512*	Caucasian
ABCA12	c.6853-5A>G	Intron/Splice site	Caucasian
ABCA12	c.4274A>G	p.Q1425R	Caucasian
ABCA12	c.2140T>C	p.R714X	N/A
ABCA12	c.6780_6781insAA	p.T227Tfs*13	Asian
ABCA12	c.2592+1G>A	Intron/Splice site	Caucasian
ABCA12	c.7664A>G	p.Q2555R	Caucasian
ABCA12	c.724_725insA	p.V242Sfs*27	Hispanic/Latino
ABCA12	c.4579+3A>G	Intron/Splice site	N/A
ABCA12	c.59_61delAAA	p.20delK	Native American
ABCA12	c.740_743delTCAG	p.V247Efs*32	Native American
ABCA12	c.2519_2520delAA	p.Q840Rfs*5	Caucasian
ABCA12	c.7332_7334delCAC	p.2445delT	Caucasian
ABCA12	c.2033_2036delATCA	p.N678Rfs*10	Caucasian
ABCA12	c.2864-6T>A	Intron/Splice site	Caucasian
ABCA12	c.451_452delG	p.G151Efs*21	Caucasian
ABCA12	c.430_431insA	p.S144Kfs*3	Caucasian
ABCA12	c.3058_3059insATATTTATTTATTTTTTTTATTTACAGG	p.A1020Ifs*17	Caucasian
ABCA12	c.1131C>G	p.Y377*	Caucasian
ABCA12	c.6481C>T	p.Q2161*	Caucasian
ABCA12	c.6200T>G	p.L2067R	Hispanic/Latino
ABCA12	c.2180delA	p.Q727Qfs*13	Hispanic/Latino
ABCA12	c.7652T>C	p.F2551S	Hispanic/Latino
ABCA12	c.7181C>A	p.T2394K	Caucasian

Gene	Nucleotide change	Amino acid change	Race/ethnicity
ABCA12	c.1414C>T	p.Q472*	Caucasian
ABCA12	c.6139_6148delGCGTTTTCAA	p.2047-2049 delAFS, p.2050I>L fs*18	Caucasian
ABCA12	c.4841G>T	p.G1614V	Caucasian
ABCA12	c.3679G>C	p.E1227Q	Caucasian
ABCA12	c.6146_6147insT	p.2046S>Ffs*16	Asian
ABCA12	c.872G>A	p.S291N	Asian
ABCA12	c.1131C>A	p.Y377*	Hispanic/Latino
ABCA12	c.313_317+9delGACAGGTGGGGGCA	p.727Q>Qfs*13	Asian
ABCA12	c.5381+1G>C	Intron/Splice site	Caucasian
ABCA12	c.2274_2275insA	p.L758Lfs*4	Black
ABCA12	c.5381+4A>G	Intron/Splice site	Caucasian
ABCA12	c.4187_4210delGGGCCTCAGCAGGCACCATTTTTG	p.GASAGTIFV1396V	Hispanic/Latino
ABCA12	c.7239+5G>A	Intron/Splice site	Hispanic/Latino
ABCA12	c.7283T>C	p.L2428P	Hispanic/Latino
ABCA12	c.5822T>G	p.L1941R	Hispanic/Latino
ABCA12	c.5260C>T	p.P1754S	Hispanic/Latino
ABHD5	c.960+5G>A	Intron/Splice site	N/A
ALDH3A2	c.1225G>C	p.A409P	Caucasian
ALOX12B	c.1109T>C	p.L370P	Caucasian
ALOX12B	c.2074C>T	p.P692S	Caucasian
ALOX12B	c.245G>C	p.W82S	Caucasian
ALOX12B	c.1353delC	p.L451Lfs*16	N/A
ALOX12B	c.1462C>T	p.R488C	Caucasian
ALOX12B	c.1350_1351insC	p.G450Gfs*28	Caucasian
ALOX12B	c.353-2A>G	Intron/Splice site	Caucasian
ALOX12B	c.291delC	p.Y97Yfs*100	Caucasian

Gene	Nucleotide change	Amino acid change	Race/ethnicity
ALOX12B	c.2061C>G	p.Y687*	Caucasian
ALOX12B	c.2058_2059insAG	p.687Y>Sfs*9	Caucasian
ALOX12B	c.673G>A	p.G225S	Hispanic/Latino
ALOX12B	c.877A>G	p.M293V	Hispanic/Latino
ALOX12B	c.2105A>G	p.*702W	Hispanic/Latino
ALOX12B	c.1755+1G>A	Intron/Splice site	Caucasian
ALOX12B	c.93G>T	p.Q31H	Caucasian
ALOX12B	c.1720T>C	p.C574R	Caucasian
ALOX12B	c.1498G>C	p.D500H	Caucasian
ALOX12B	c.631_633delTTC	p.211delF	Black
ALOX12B	c.340C>T	p.R114w	Hispanic/Latino
ALOX12B	c.311G>A	p.W104*	Hispanic/Latino
ALOX12B	c.1A>G	p.M1V	Native American
ALOX12B	c.1532+4A>G	Intron/Splice site	Native American
ALOX12B	c.214G>T	p.E72*	Caucasian
ALOX12B	c.406_408delGAG	p.136delE	Hispanic/Latino
ALOX12B	c.772T>C	p.W258R	Caucasian
ALOX12B	c.1498G>T	p.D500Y	Caucasian
ALOX12B	c.190C>T	p.L64F	Caucasian
ALOX12B	c.1273_1274insG	p.K425Efs*24	Hispanic/Latino
ALOX12B	c.406_408delCTC	p.136delE	Caucasian
ALOX12B	c.242delC	p.81P>Lfs*116	Caucasian
ALOX12B	c.1600C>T	p.Q534*	Caucasian
ALOX12B	c.1325G>A	p.R442Q	Caucasian
ALOX12B	c.G1579A	p.V527M	Caucasian
ALOXE3	c.2181+2T>G	Intron/Splice site	Caucasian
ALOXE3	c.2466C>G	p.N822K	Caucasian

Gene	Nucleotide change	Amino acid change	Race/ethnicity
ALOXE3	c.599G>C	p.R200P	Caucasian
ALOXE3	c.1348_1349insC	p.450L>Pfs*58	Caucasian
ALOXE3	c.830+1G>T	Intron/Splice site	Caucasian
ALOXE3	c.1076+1C>T	Intron/Splice site	Caucasian
ALOXE3	c.2377G>T	p.E793*	Caucasian
ALOXE3	c.2360delT	p.L787R	Caucasian
ALOXE3	c.2203C>G	p.P735A	Hispanic/Latino
ALOXE3	c.748G>C	p.A250P	Hispanic/Latino
ATP2A2	c.2828A>G	p.H943R	N/A
ATP2A2	c.669_670insG	p.V223Vfs*7	Caucasian
ATP2A2	c.1334T>C	p.L445P	Caucasian
ATP2A2	c.1484C>T	p.S495L	Hispanic/Latino
ATP2C1	c.2477_2480delTTGT	p.F826Sfs*10	N/A
ATP2C1	c.1510C>T	p.Q505*	Caucasian
ATP2C1	c.2872delC	p.P958Pfs*9	Caucasian
ATP2C1	c.1471G>T	p.E491*	Hispanic/Latino
ATP2C1	c.1037T>C	p.I346T	Caucasian
ATP2C1	c.1327_1328insAC	p.C443Tfs*8	Caucasian
ATP2C1	c.42C>A	p.N14K	Caucasian
ATP2C1	c.277delG	p.G93Afs*38	Caucasian
ATP2C1	c.1515+1 G>A	splice site	Caucasian
CAST	c.454C>T	p.Q152*	Hispanic/Latino
CDSN	c.85G>C	p.G29R	Black
CDSN	c.418C>A	p.H140N	N/A
CDSN	c.447-449del AAG	p.GS149G	Caucasian
CERS3	c.47T>G	p.L16R	Hispanic/Latino
CERS3	c.223C>T	p.R75*	Hispanic/Latino

Gene	Nucleotide change	Amino acid change	Race/ethnicity
CYP4F22	c.1043T>C	p.L348P	Native American
CYP4F22	c.491A>C	p.H164P	Native American
CYP4F22	c.215T>C	p.L72P	Hispanic/Latino
CYP4F22	c.15_19delAGACC	p.T5Tfs*73	Caucasian
CYP4F22	c.980delC	p.A327Afs*43	N/A
CYP4F22	c.1012G>T	p.D338Y	Caucasian
CYP4F22	c.58_59insG	p.R20Rfs*60	Caucasian
CYP4F22	c.59_60insG	p.R20Rfs*60	Caucasian
DSC2	c.C1264T	p.P422S	Hispanic/Latino
DSG1	c.313delA	p.K105Kfs*7	Caucasian
DSG1	c.1892G>C	p.G631A	Caucasian
DSG1	c.337ins T	p.113S>Ffs*4	Black
EBP	c.473A>G	p.Q158R	Caucasian
EBP	c.340_341insAAACT	p.E114Gfs*26	Caucasian
ELOVL1	c.494C>T	p.S165F	Caucasian
GJB2	c.263C>T	p.A88V	Caucasian
GJB2	c.134G>C	p.G45A	Asian
GJB2	c.42C>A	p.N14K	Caucasian
GJB2	c.148G>A	p.D50N	Asian
GJB2	c.83T>A	p.L28H	Caucasian
GJB3	c.625C>T	p.L209F	Caucasian
KRT1	c.1455_1457delCCT	p.486delL	Asian
KRT1	c.1752_1753insG	p.S584Rfs	Native American
KRT1	c.592G>A	p.V198M	N/A
KRT1	c.1016delT	p.M339Rfs*23	Hispanic/Latino
KRT1	c.575C>A	p.A192D	N/A
KRT1	c.562A>C	p.N188H	N/A

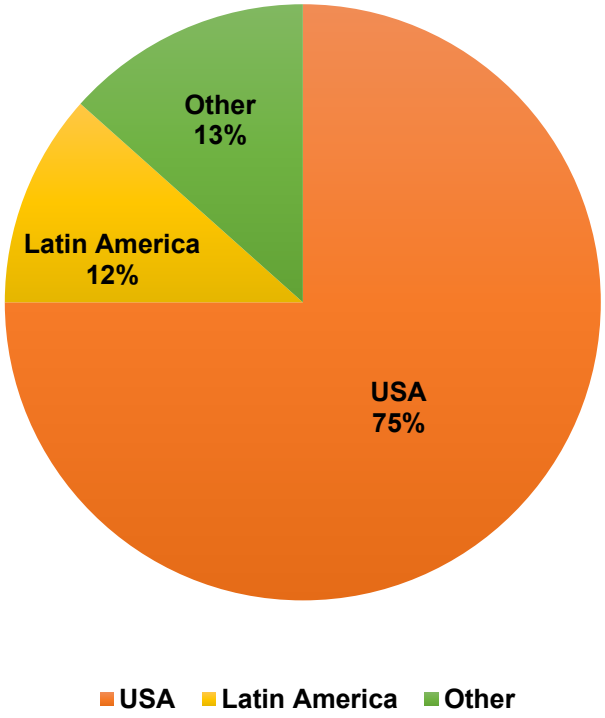
Gene	Nucleotide change	Amino acid change	Race/ethnicity
KRT1	c.1539delT	p.S513Rfs*100	Caucasian
KRT1	c.1430T>C	p.L477P	N/A
KRT1	c.T584A	p.I195N	Black
KRT10	c.1373delG	p.S458I	Caucasian
KRT10	c.1301_1303delAAC	p.434delQ	Caucasian
KRT10	c.1547_1548insG	p.G516Gfs*65	Caucasian
KRT10	c.1374-2A>C	Intron/Splice site	Caucasian
KRT10	c.1373+1G>A	Intron/Splice site	Native American
KRT10	c.1374-1G>C	Intron/Splice site	Native American
KRT10	c.1364_1365delGA	p.G455Gfs*125	Caucasian
KRT10	c.1345T>C	p.Y449H	N/A
KRT10	c.458T>C	p.L153P	N/A
KRT10	c.1467_1478delCGGCCACGGCGG	p.G489G	Caucasian
KRT10	c.1322G>C	p.R441P	Caucasian
KRT10	c.950_951insCT	p.L317Pfs*3	Caucasian
KRT10	c.1521_1536delAAGCTCCGGCGGCGGC	p.G507G	Caucasian
KRT10	c.1361_1365delAAGGA	p.E454Gfs*125	N/A
KRT10	c.1373+1G>C	Intron/Splice site	N/A
KRT10	c.1373+2T>G	Intron/Splice site	Caucasian
KRT10	c.1348_1389insC	p.R450Pfs*131	Caucasian
KRT10	c.460A>G	p.N154D	Caucasian
KRT10	c.1305_1307delCCT	p.436delL	N/A
KRT10	c.1566_1567insAAGCTCCAGCGGCGGCCAC	p.G523Kfs*64	Hispanic/Latino
KRT10	c.1307T>C	p.L436P	Caucasian
KRT10	c.1345T>A	p.Y449N	Caucasian
KRT10	c.1668_1669insG	p.G556Gfs*25	Caucasian
KRT10	c.470C>T	p.P157L	Caucasian

Gene	Nucleotide change	Amino acid change	Race/ethnicity
KRT10	c.998G>A	p.R33H	Caucasian
KRT10	c.551T>C	p.I184T	Black
KRT10	c.1084G>A	p.A362T	Caucasian
KRT10	c.862G>A	p.E288K	Asian
KRT2	c.126C>G	p.C42W	N/A
KRT2	c.1430T>A	p.I477N	Hispanic/Latino
KRT2	c.558C>G	p.N186K	Caucasian
KRT2	c.561-563delCAA	p.NK187K	Caucasian
KRT2	c.1912T>C	p.F638L	Caucasian
LOR	c.672dupT	p.Y225Lfs*111	N/A
LSS	c.1417dup C	p.H473Pfs*32	Caucasian
MBTPS2	c.686T>C	p.F229S	Asian
MBTPS2	c.1427T>C	p.L476S	Caucasian
NIPAL4	c.463+5G>T	Intron/Splice site	Hispanic/Latino
NIPAL4	c.187A>G	p.M63V	Caucasian
NIPAL4	c.555C>A	p.Y185*	Native American
NIPAL4	c.527C>A	p.A176D	Caucasian
NSDHL	c.308A>G	p.H103R	Caucasian
NSDHL	c.612-613insT	p.G205Wfs*66	N/A
PNPLA1	c.448T>C	p.S140P	Hispanic/Latino
PNPLA1	c.448T>C	p.C150R	Hispanic/Latino
PNPLA1	c.1296delG	p.V432Vfs*24	Asian
PNPLA1	c.362A>C	p.H121P	Caucasian
PNPLA1	c.440C>G	p.A147G	Caucasian
PNPLA1	c.939_951delGTGGGTTCCCAAA	p.EWVPK314-317Efs*50	Asian
PNPLA1	c.421A>G	p.K46E	Asian
PNPLA1	c.157T>C	p.S53P	Hispanic/Latino

Gene	Nucleotide change	Amino acid change	Race/ethnicity
PNPLA1	c.158C>G	p.S53W	Asian
PNPLA1	c.143G>C	p.R48P	Caucasian
PNPLA1	c.500G>T	p.G167V	Hispanic/Latino
PNPLA1	c.272delC	p.S91Sfs*9	Caucasian
PNPLA1	c.775+2T>C	Intron/Splice site	Caucasian
RSPO1	c.291C>A	p.C97*	Asian
SDR9C7	c.364_365insA	p.T122Nfs*4	Middle Eastern
SNAP29	c.355_356insG	p.119insL	Hispanic/Latino
SPINK5	c.316_317delGA	p.D106Wfs*7	Caucasian
SPINK5	c.238_239insG	p.A80Gfs*19	Caucasian
SPINK5	c.140A>G	p.D47G	N/A
SPINK5	c.2459_2462delAAAA	p.E820Efs*121	N/A
SPINK5	c.2469delG	p.K823Kfs*119	N/A
SPINK5	c.81+2T>A	Intron/Splice site	N/A
SPINK5	c.2577_2578delA	p.G859Gfs*83 (c.2577), p.K860Sfs*82 (c.2578-2579)	N/A
SPINK5	c.2425_2426insT	p.M809Yfs*3	N/A
SPINK5	c.81+5G>A	Intron/Splice site	N/A
SPINK5	c.411_1delG	Intron/Splice site	N/A
SPINK5	c.235_236insG	p.R79Rfs*20	Hispanic/Latino
SPINK5	c.1346_1347delTT	p.L449Lfs*7	Asian
SPINK5	c.2459_2460insA	p.E820Efs*8	Caucasian
SPINK5	c.1086_1087delAT	p.S362Sfs*7	Caucasian
SPINK5	c.2259_2260insA	p.R753Rfs*4	Caucasian
SPINK5	c.2577delA	p.G859Gfs*83	Caucasian
SPINK5	c.2029-2039 del GAGGAAAGAAA	p.677-680EERK>EERRfs*29	Middle Eastern
ST14	c.737G>C	p.R221C	Asian
TGM1	c.2149delC	p.L717Ffs*34	Hispanic/Latino

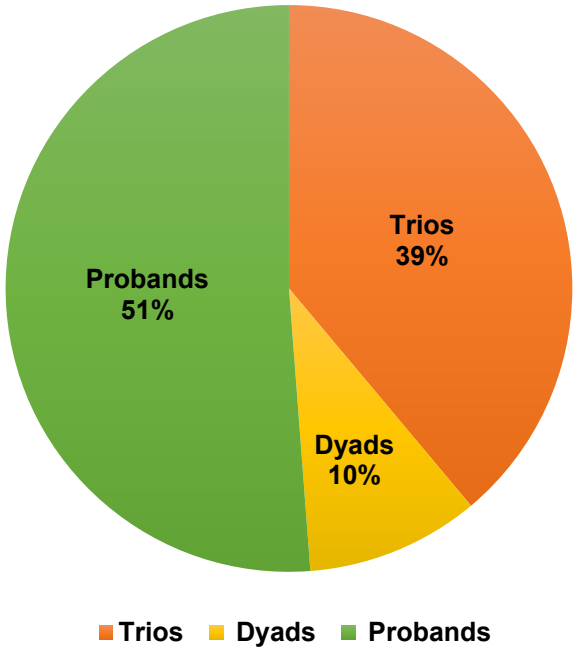
Gene	Nucleotide change	Amino acid change	Race/ethnicity
TGM1	c.443_449delATATGCT	p.H148Pfs*32	Asian
TGM1	c.1294G>T	p.R432*	Asian
TGM1	c.407_408insAGTATGAGTA	p.Y136*	Caucasian
TGM1	c.411_412insCGAC	p.E138Rfs*22	Caucasian
TGM1	c.698_699insT	p.F233Ffs*6	Asian
TGM1	c.411_412insCGAC	p.E137Dfs*22	Caucasian
TGM1	c.1121A>G	p.PY374C	Caucasian
TGM1	c.713delA	p.D238Afs*92	Hispanic/Latino
TGM1	c.1504A>T	p.K502*	Hispanic/Latino
TGM1	c.1097T>C	p.L366P	N/A
TGM1	c.886_889delGG	p.G296Gfs*38	N/A
TGM1	c.1223_1228delACACAT	p.R396H	Caucasian
TGM1	c.443delA	p.H148Lfs*34	N/A
TGM1	c.278delG	p.G93Afs*17	Caucasian
TGM1	c.1160-2A>C	Intron/Splice site	Caucasian
TGM1	c.1420C>T	p.P474S	Caucasian
TGM1	c.2324T>G	p.L775R	Hispanic/Latino
TGM1	c.985-3C>G	Intron/Splice site	Caucasian
TGM1	c.1738G>A	p.A580T	Caucasian
TGM1	c.527C>A	p.G273R	Caucasian
TGM1	c.394_396delGAC	p.132delD	Asian
TGM1	c.1483T>C	p.F495L	Caucasian
TGM1	c.1956C>A	p.Y652*	Hispanic/Latino
TGM1	c.379C>T	p.R127*	Hispanic/Latino
TGM1	c.1552delG	p.V518Wfs*40	Black
TGM1	c.834delG	p.G278Gfs*52	Asian
TGM1	c.2226-2A>G	Intron/Splice site	Asian

Gene	Nucleotide change	Amino acid change	Race/ethnicity
TGM1	c.1159+1G>T	Intron/Splice site	Hispanic/Latino
TGM1	c.1223_1227delACACA	p.D408Vfs*21	Hispanic/Latino
TGM1	c.1018delG	p.G340Gfs*44	Caucasian
TGM1	c.2320C>T	p.Q774*	Caucasian
TGM1	c.1271_1272insT	p.L424Lfs*7	Middle Eastern
TGM1	c.1646G>A	Intron/Splice site	Middle Eastern
TGM1	c.1086_1091delGCTTAG	p.362_363delLS	Middle Eastern
TGM1	c.802delG	p.V268Ffs*62	Middle Eastern
TGM1	c.373A>G	p.N125D	N/A
TGM1	c.1448G>T	p.G483V	Caucasian
TGM1	c.1921_1927+3delGGGGCCTGTA	Intron/Splice site	Asian
TGM1	c.832G>C	p.G278R	Hispanic/Latino
TGM1	c.1645G>A	p.G549S	Hispanic/Latino
TGM1	c.1096C>G	p.L366V	Asian
TGM1	c.1226_1227delCA	p.T409Ifs*21	Caucasian
TGM1	c.411_412insCGAC	p.D137Rfs*22	Caucasian
TGM1	c.1196C>T	p.T399I	Asian
TGM1	c.757+1G>T	Intron/Splice site	Hispanic/Latino
TGM1	c.1233_1234insA	p.T411Yfs*19	Hispanic/Latino
TGM1	c.456_458delCCT	p.LL152L	Black
TGM1	c.890T>C	p.V297A	Caucasian
TGM1	c.391A>G	p.T131A	Asian
TGM1	c.1130G>A	p.A176D	Caucasian
TGM1	c.2060G>A	p.R687H	Asian
TGM1	c.C427T	p.R143C	Hispanic/Latino
TGM1	c.877-2T>C	Intron/Splice site	Caucasian



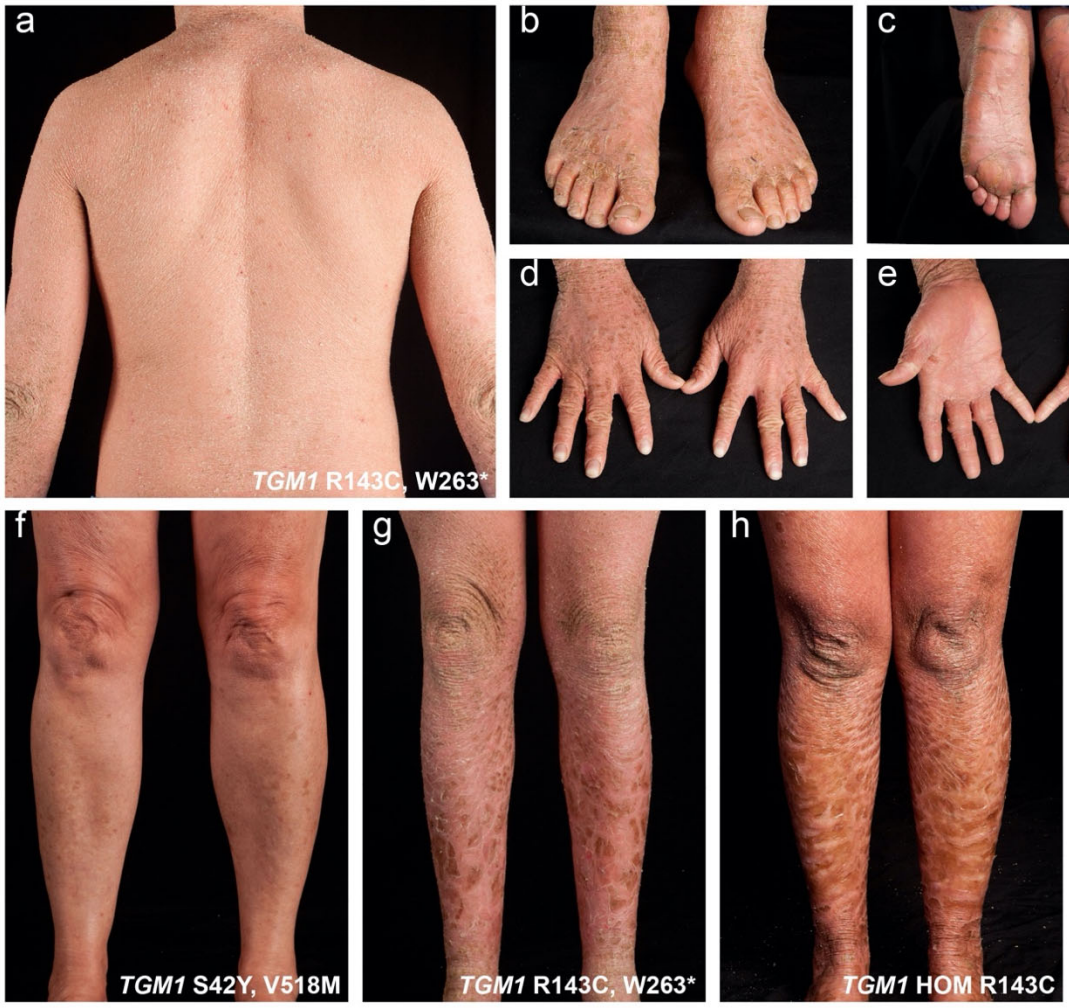
eFigure 1. Geographic distribution of 1000 kindreds

Among the 1000 kindreds analyzed, 750 (75%) were from the USA, 116 (12%) were from Latin America, and 134 were from Other regions, including Canada (4%), Europe (3%), Asia (3%), Africa (2%), Middle East (1%) and Australia and New Zealand (1%).



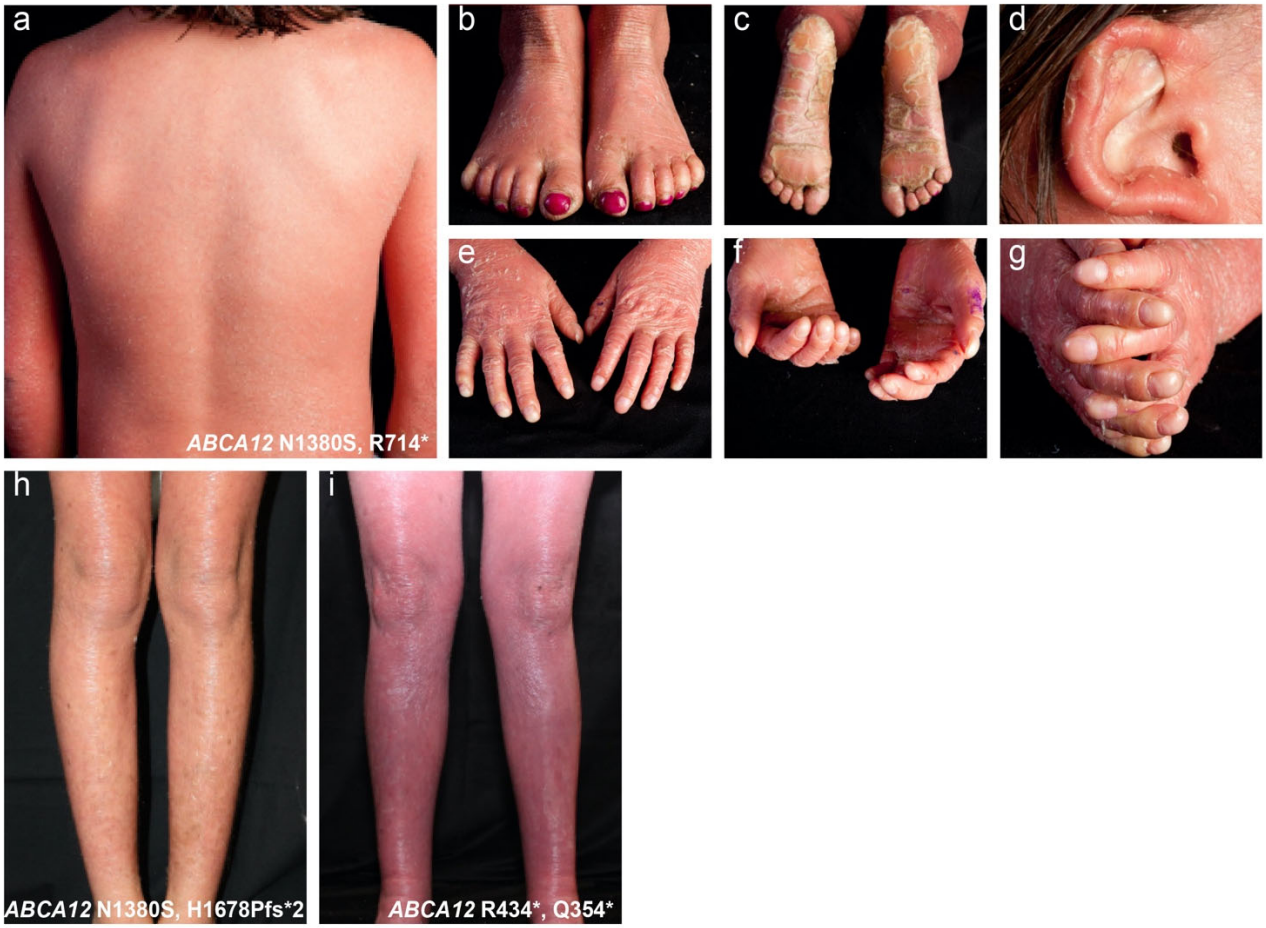
eFigure 2. Distribution of trios, dyads and probands among 1000 kindreds

Among the 1000 kindreds analyzed, 389 (39%) were trios (index case and both parents), 99 (10%) were dyads (index case and one parent) and 512 (51%) were probands only.



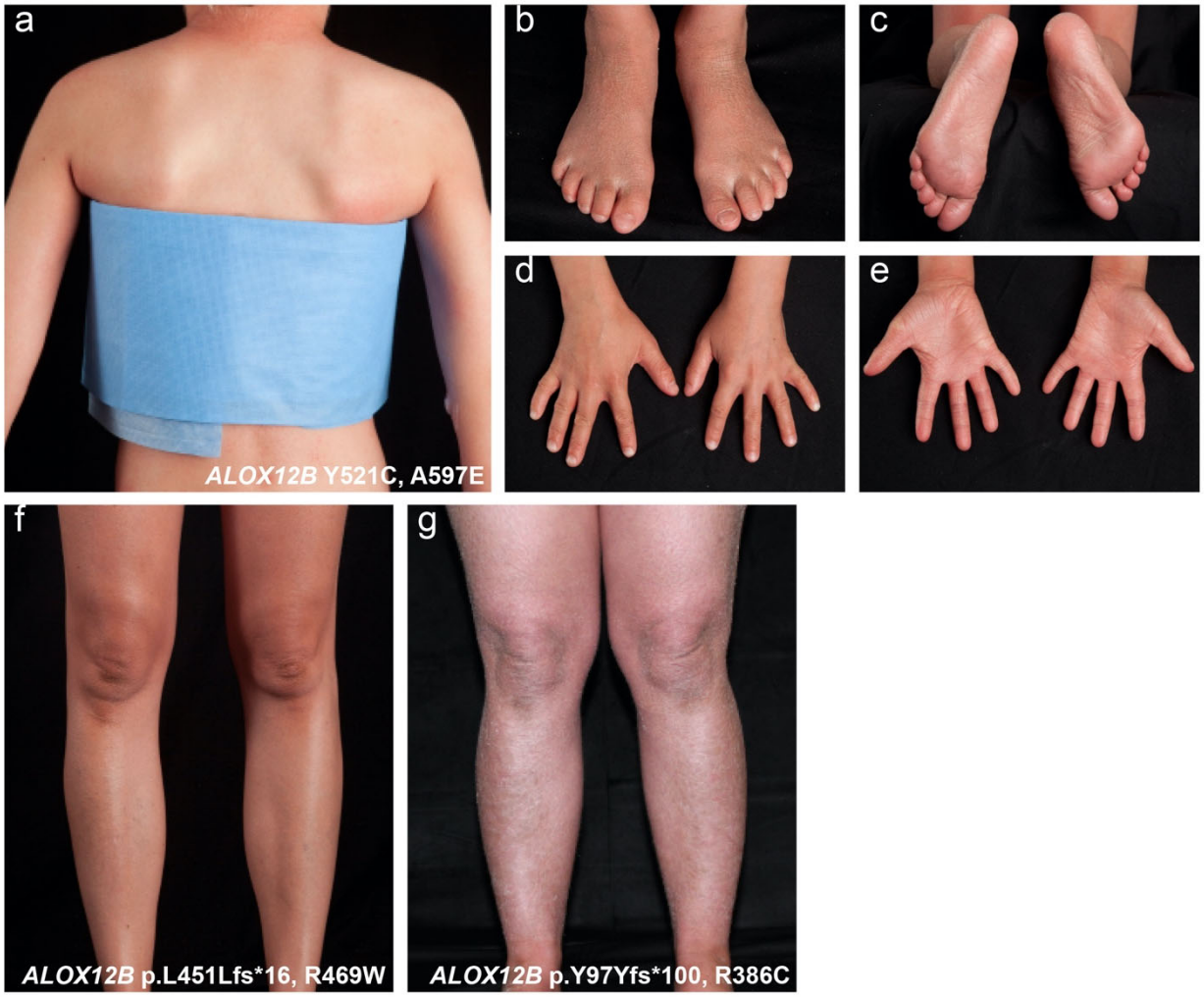
eFigure 3. Phenotypes of ARCI due to *TGM1* mutations

(a-e) The characteristic appearance of subjects with *TGM1* mutations include flat, plate-like scales in a mosaic pattern and mild to moderate erythema. Phenotypes range from discontinuous smoothening (diminished fine skin markings, shininess) **(f)**, confluent scales with pink erythema **(g)**, and confluent, primarily large (>1cm) plate-like thick scales. The largest and darkest scales tend to be on the lower extremities **(h)**.



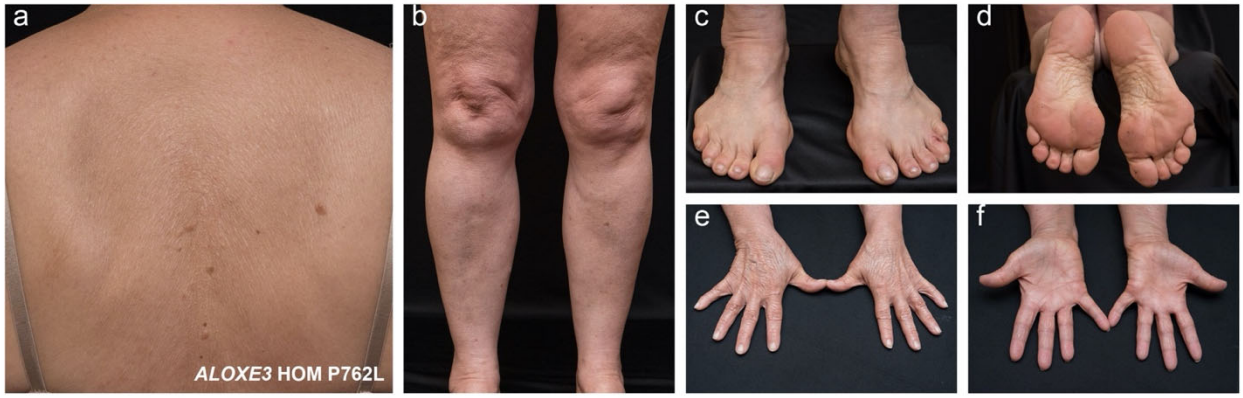
eFigure 4. Phenotypes of ARCI due to *ABCA12* mutations

(a-e) The characteristic appearance of ichthyosis caused by *ABCA12* mutations include significant and often severe erythema with fine white or thick lamellar scale and PPK. **(d-g)** *Distinguishing features* include tapered digits, hyperconvex nails, and pyknotic ears. Clinical manifestations range from mild erythema and discontinuous smoothening with small scales **(h)** to severe erythema with confluent smoothening and large scales **(i)**.



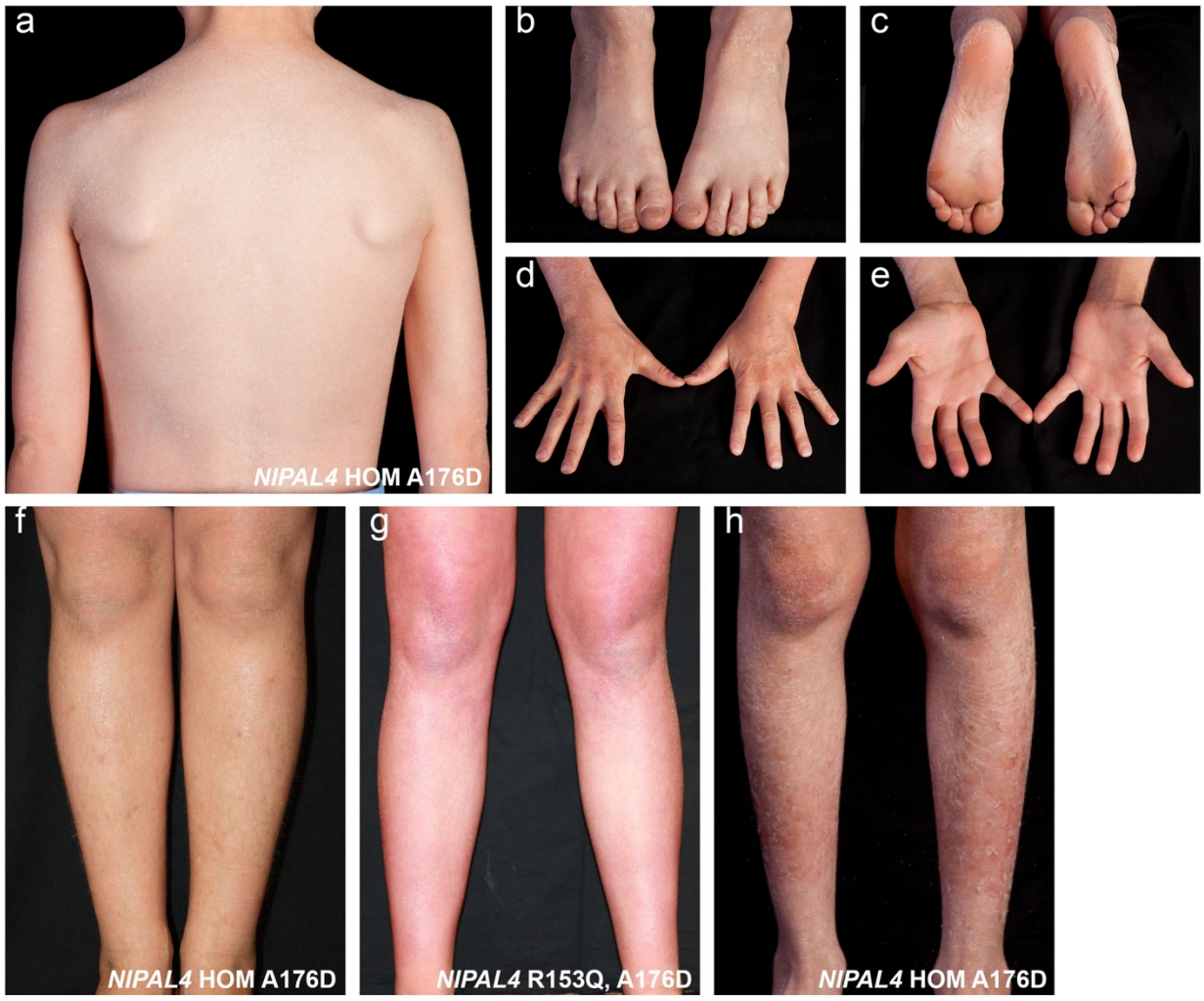
eFigure 5. Phenotypes of ARCI due to *ALOX12B* mutations

(a-e) The characteristic appearance of ichthyosis caused by mutations in *ALOX12B* include fine scale, absence of PPK, and erythema that is mild in some subjects. Phenotypic manifestations range from discontinuous smoothening with absence of erythema **(f)** to confluent fine scale and pink erythema **(g)**.



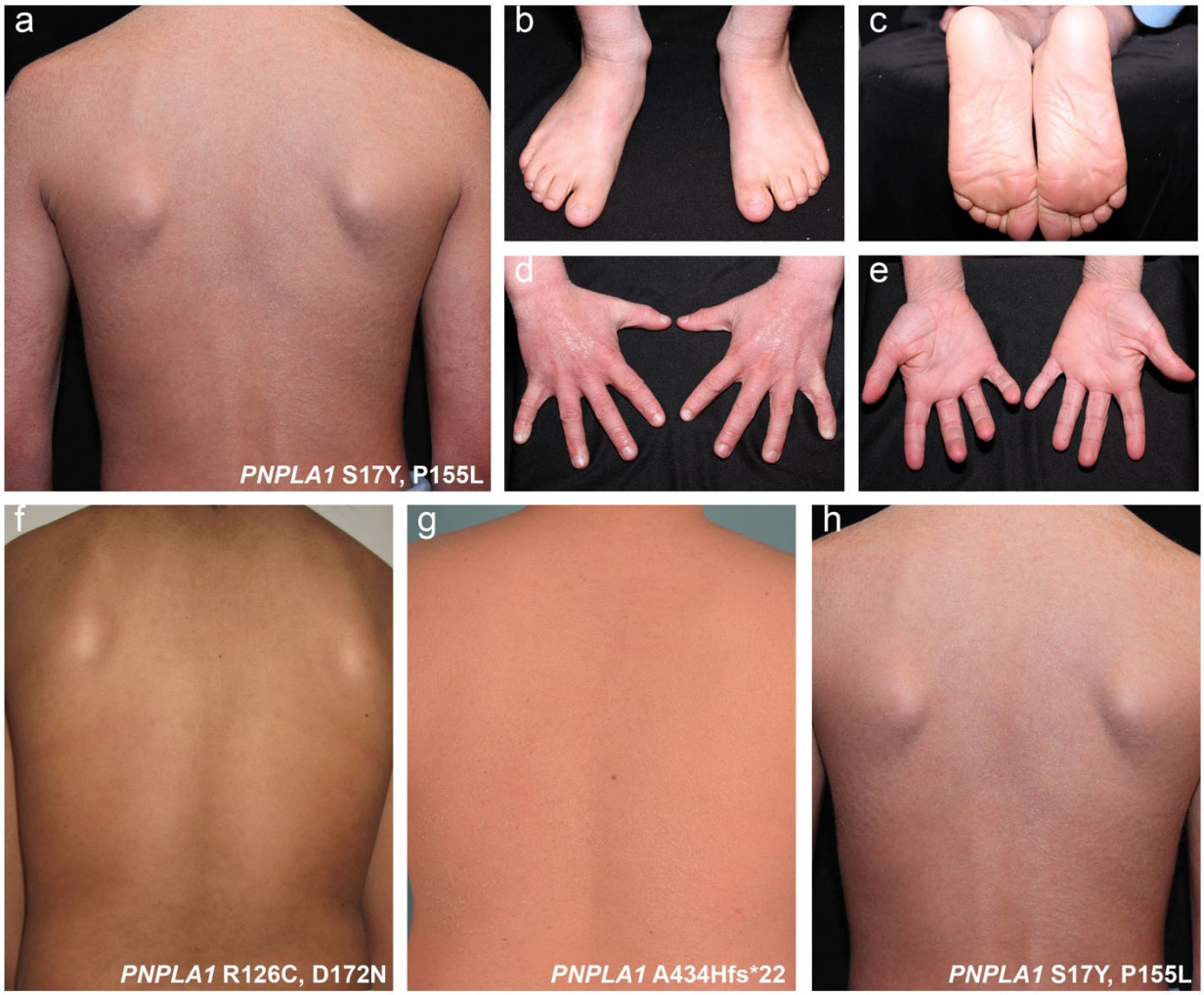
eFigure 6. Phenotypes of ARCI due to *ALOXE3* mutations

(a-f) Similar to *ALOX12B* mutations, the characteristics of ichthyosis caused by *ALOXE3* mutations include fine scale, absence of PPK, and minimal to mild erythema. There was minimal variation of these features among subjects.



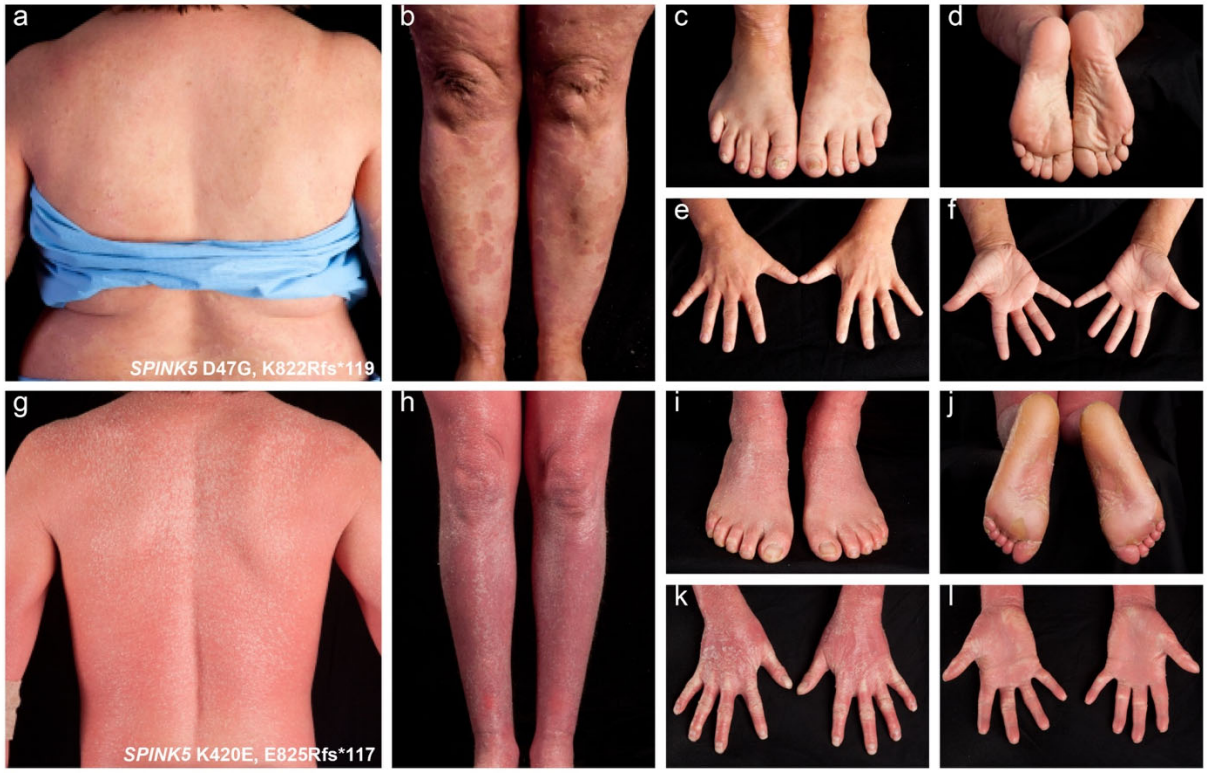
eFigure 7. Phenotypes of ACRI due to *NIPAL4* mutations

(a-e) The characteristic appearance of ichthyosis caused by mutations in *NIPAL4* include fine scale, absence of PPK, and a varying degree of erythema. The range of clinical manifestations includes barely perceptible pink erythema with discontinuous smoothening **(f),** pink/red erythema with confluent, fine, white scale **(g)** and pink erythema with confluent scale, including some large (>1cm) scale **(g)**. The 3 subjects in **a-e**, **f**, and **h** are homozygous for *NIPAL4* p.A176D.



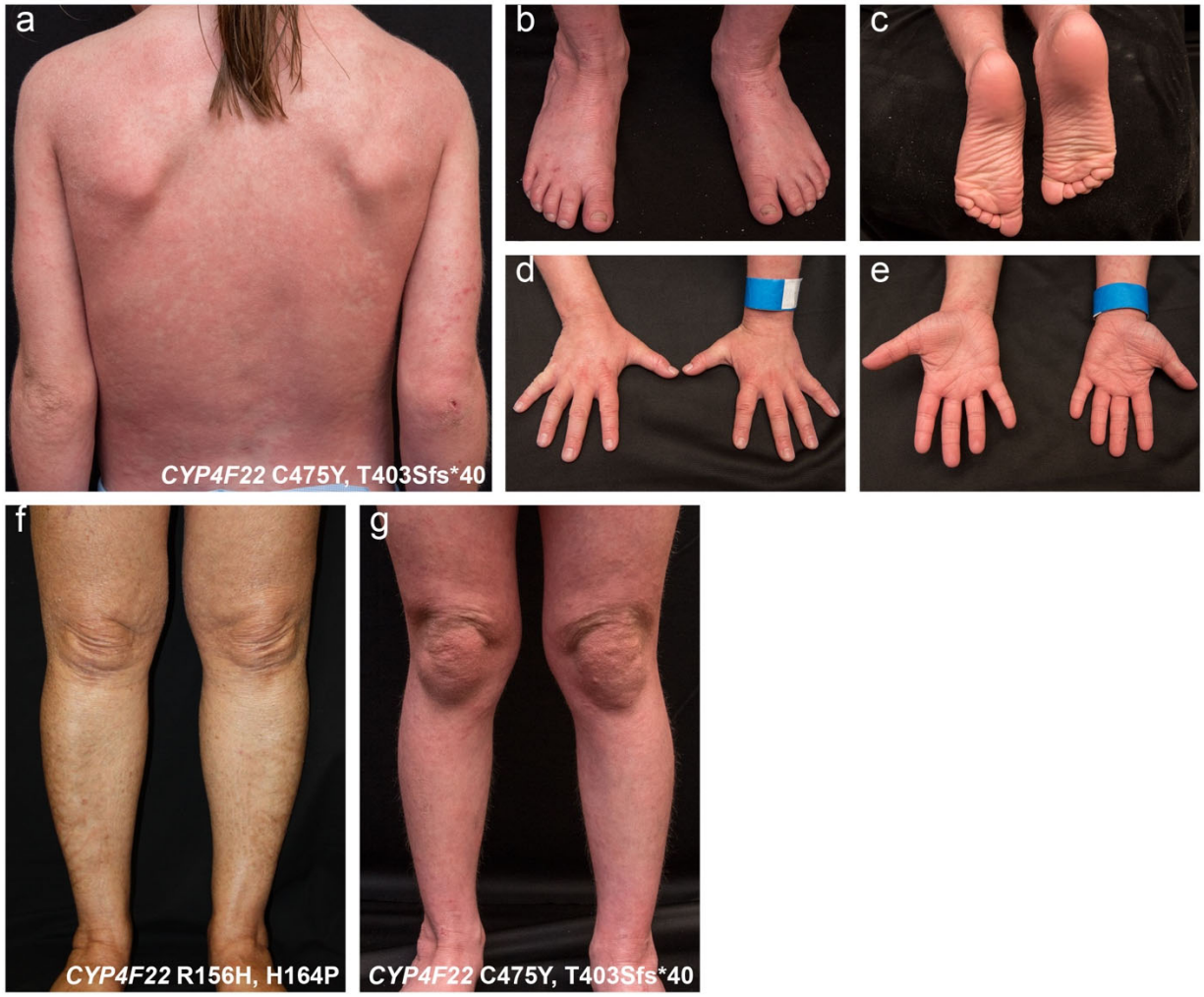
eFigure 8. Phenotypes of ARCI due to *PNPLA1* mutations

(a-e) The characteristic appearance of ichthyosis caused by mutations in *PNPLA1* included fine or plate-like scale and a varying degree of erythema. PPK was most often absent, but mild when present. The range of phenotypic manifestations included mild to moderate erythema with fine white scale **(f-g)** and mild erythema with more severe scale **(h)**.



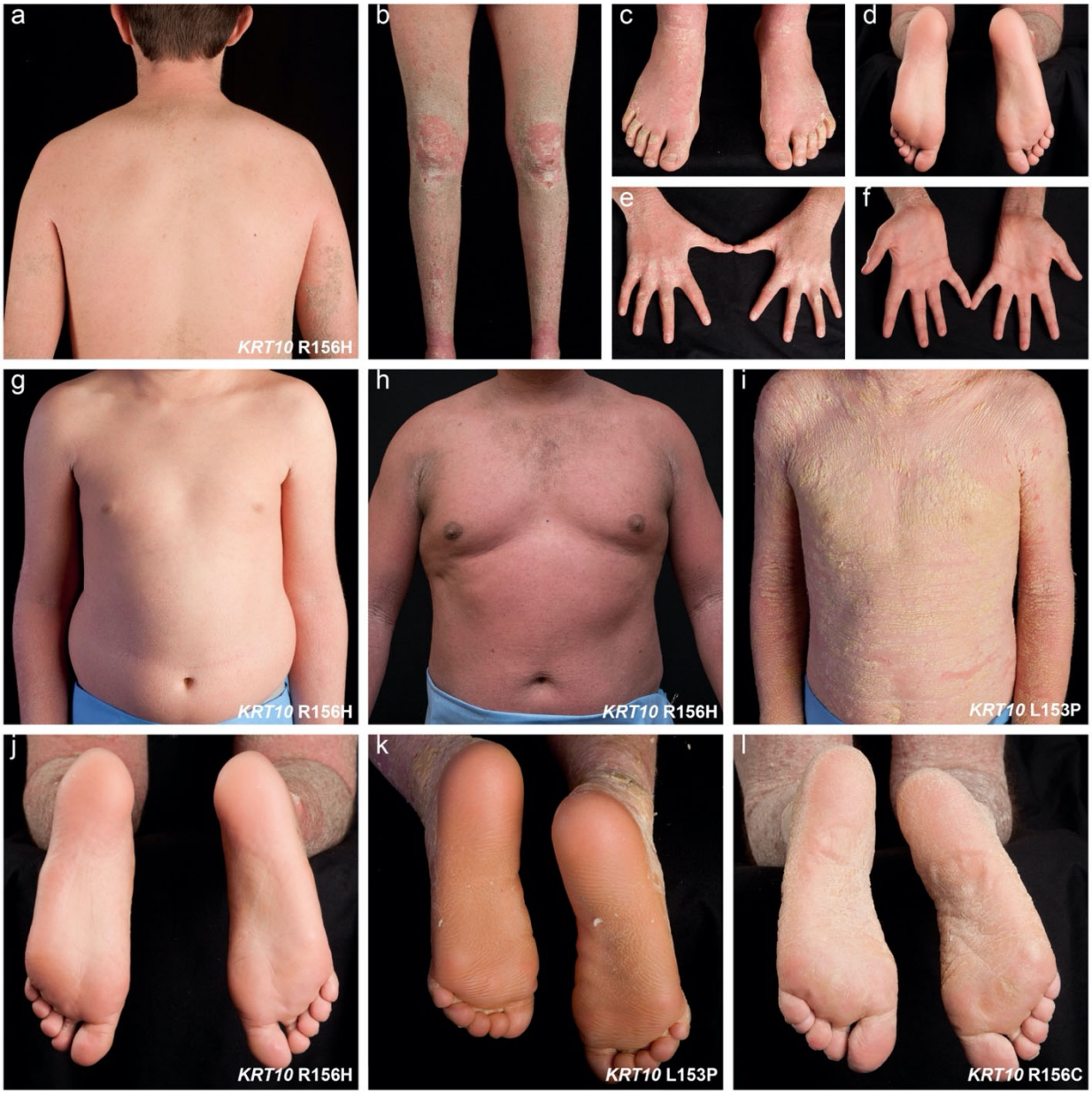
eFigure 9. Phenotypes of Netherton syndrome due to *SPINK5* mutations

(a-f) The *distinguishing feature* of ichthyosis caused by *SPINK5* mutations is ichthyosis linearis circumflexa (ILC), which presents as polycyclic erythematous plaques with a double-edge configuration. However, ichthyosis caused by *SPINK5* mutations can also resemble CIE. **(g-l)** This subject has characteristic findings of CIE, including severe erythema with fine white scale and moderate PPK.



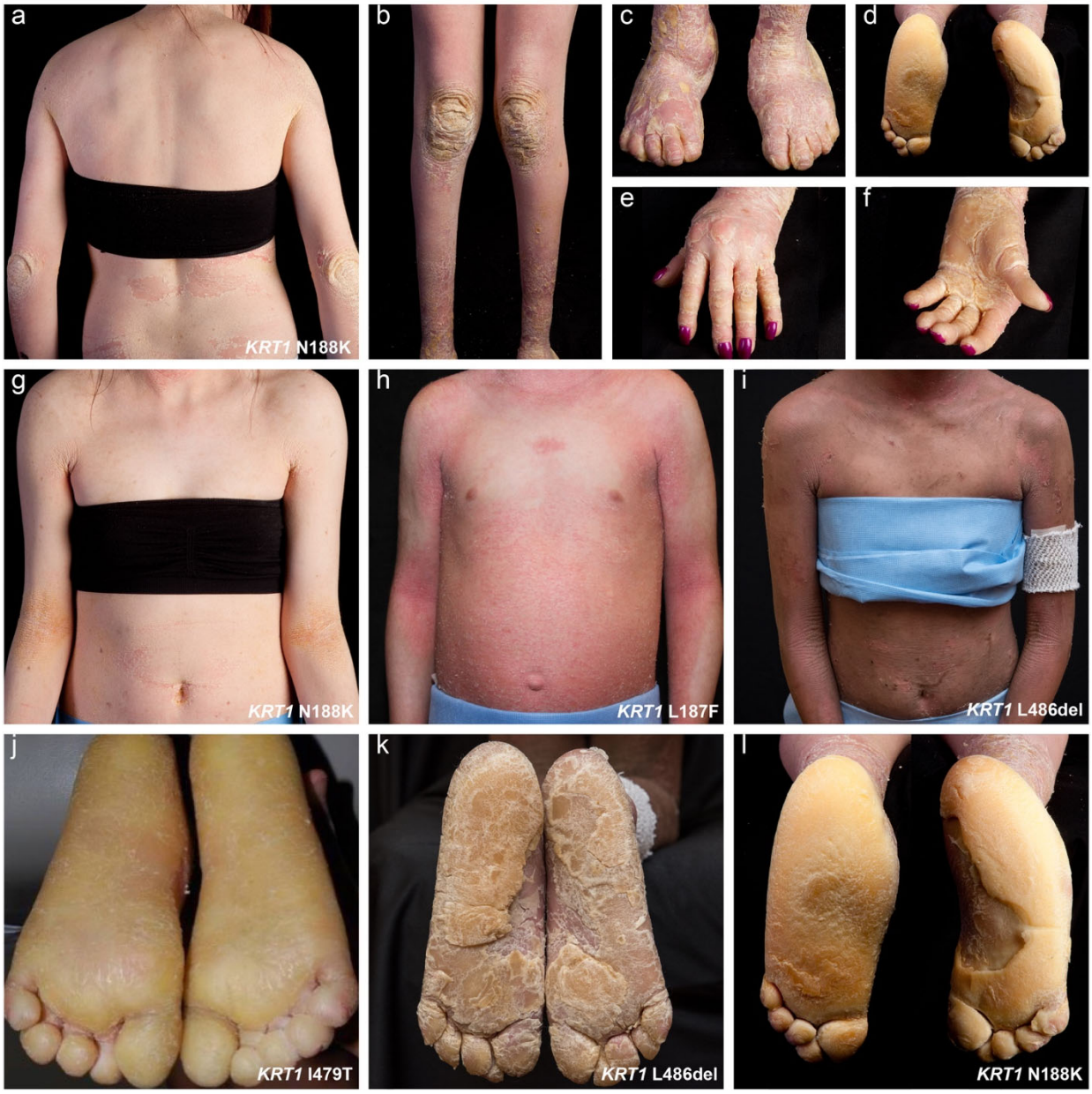
eFigure 10. Phenotypes of ARCI due to *CYP4F22* mutations

(a-e) The characteristic appearance of ichthyosis caused by mutations in *CYP4F22* include fine, white or plate-like scale, mild to severe erythema, and absence of PPK. Phenotypic manifestations range from imperceptible pink erythema and plate like scale **(f)** to moderate to severe erythema with fine, white scale **(g)**.



eFigure 11. Phenotypes of EI due to *KRT10* mutations

(a-f) The characteristic appearance of ichthyosis caused by mutations in *KRT10* include columns of scale and skin fragility, especially at sites of trauma. The range of skin findings include discontinuous regions of hyperkeratotic surface accentuation, including organized or geometric exaggeration of coarse skin markings **(g)** to pink/red erythema with scale primarily in intertriginous areas **(h)**, and confluent, white/yellow columns of scale **(i)**. **(j-1)** PPK, when present, is smooth with occasional focal accentuation.



eFigure 12. Phenotypes of EI due to *KRT1* mutations

The characteristic appearance of ichthyosis caused by *KRT1* mutations included skin fragility, especially at sites of trauma, and columns of scale that is accentuated over the extensor surfaces of joints, particularly knees and elbows. **(a-f)** *Distinguishing features* included thick, often functionally limiting PPK. Skin findings ranged from columns of scale most prominent in the intertriginous areas and mild erythema **(g)** to confluent, organized or geometric exaggeration of coarse skin markings with pink erythema and marked skin fragility **(h and i)**. There was significant PPK in all cases, ranging from moderate and smooth (**j**), moderate and patchy (panel **k**), to severe and smooth PPK (panel **l**).