Table SII. *Summary of clinical and mutational data in 26 families with mutations in* KRT1, KRT2 *and* KRT10 *(novel mutations shown in* **bold***)*

Family/pat./ Sex, age, years	Pheno-type	Gene	Exon/ Intron	Mutation	Clinical and histological findings
P1/M, 14	SEI	*KRT2*	Ex1	c.558C>A p.Asn186Lys	Blisters in neonatal period. Mild to moderate hyperkeratosis and bullous lesion in summer and in case of significant friction. Histology: acanthosis, hyperkeratosis and parakeratosis, cytolysis and loss of cohesion in the upper stratum spinosum and stratum granulosum
P2-1/M, 42	SEI	*KRT2*	Ex7	**c.1438T>C p.Tyr480His**	Mild hyperkeratosis, Bullous phenotype stopped at puberty. Histology: Acanthosis, orthokeratotic hyperkeratosis, vacuolar degeneration of superficial keratinocytes
P2-2/M, 9					Mild hyperkeratosis, Bullous lesions in summer only. Histology: Acanthosis, orthokeratotic hyperkeratosis, vacuolar degeneration of superficial keratinocytes
P3-1/M, 65	SEI	*KRT2*	Ex7	c.1459G>A p.Glu487Lys	Typical SEI, no additional features described
P3-2/M, 31					Typical SEI, no additional features described
P3-3/F, 29					Typical SEI, no additional features described
P4/M, 30	SEI	*KRT2*	Ex7	c.1459G>A p.Glu487Lys	Moderate SEI, blister formation at birth. Ichthyosis is pronounced after the joints. Hands and feet are spared. His father shows mild SEI, which is pronounced on lower legs and which responded well to treatment with acitretin. Face, hands and feet are spared (DNA not tested)
P5/F, 17	EI	*KRT1*	Ex1	c.563A>G p.Asn188Ser	Severe PPK, generalized ichthyosis, pronounced at extensor side of the joints
P6/M, 2	EI	*KRT1*	Ex2	c.698C>T p.Ser233Leu	Epidermolytic PPK Type Vörner. Progredient PPK. Improvement in summer
P7/M, 39	EI	*KRT1*	Ex7	c.1434G>T p.Glu478Asp	Mild EI confirmed by ultrastructure as well as histology, recurrent blistering, pruritus, pronounced epidermolytic PPK. Good treatment response to years of corticosteroid therapy. Daughter (DNA not tested): generalized EI, she was born with bullous ichthyosiform erythroderma. Hands and feet are involved showing development of PPK
P8-1/F, 2	EI	*KRT1*	Ex7	c.1436T>C p.Ile479Thr	Vesicles and superficial blisters with surrounding erythema in neonatal period, leading to a peeling aspect of the skin predominantly on arms, thighs, gluteal palmoplantar and genitoanal area, sparing the face and trunk. Blistering declined after 2–3 months, was still present in the genitoanal area but only occurred on the extremities after mechanical stress. Meanwhile she developed hyperkeratosis on hands and feet as well as knees
P8-2/M, 34					Blistering stopped at the age of 5–6 years, whereas hyperkeratotic manifestations persisted predominantly on the hands and feet
P9/F, 37	EI	*KRT1*	Ex7	c.1468G>A p.Glu490Lys	Bullous ichthyosiform erythroderma at birth with erosions, improvement with age. In adulthood, generalized ichthyosis with mild erythema and pruritus. Histology: mild acanthosis, hyperkeratosis, blisters in the suprabasal layers of the epidermis
P10/M, 50	EI	*KRT1*	Ex9	**c.1752dupT p.Gly585Trpfs69***	Ichthyosis from birth, at age of 50 years: moderate PPK, generalized ichthyosis, pronounced at extensor side of the joints. Improvement in summer. Several family members in 4 generations affected (DNA not tested)
P11/M, 0 (2d)	EI	*KRT10*	Ex1	c.466C>T p.Arg156Cys	Blistering and erosions at birth, mild EI. Histology: mild acanthosis, hyperkeratosis, vacuolar degeneration of suprabasal keratinocytes
P12-1/M, 2	EI	*KRT10*	Ex1	c.467G>A p.Arg156His	Bullous ichthyosiform erythroderma at birth
P12-2[1]/F, 34				c.467G>A p.Arg156His (mosaic)	Less affected than her son. Bullous ichthyosiform erythroderma at birth, but fewer blisters than her son. By now blistering and hyperkeratosis only occur after mechanical stress. She has arterial hypertension since her mid-20s and Hashimoto thyroiditis
P13/F, 30	EI	*KRT10*	Ex1	c.467G>A p.Arg156His	Typical EI, no additional features described
P14/M, 36	EI	*KRT10*	Ex1	c.467G>A p.Arg156His	Moderate EI. Bullous ichthyosiform erythroderma at birth, improvement in childhood. Adulthood: generalized hyperkeratosis and scaling with mild erythema. Hands and feet: mild hyperlinear phenotype similar to ichthyosis vulgaris, no PPK. Daughter (DNA not tested): classical EI with pronounced hyperkeratosis over the joints. Hands and feet are spared
P15/F, 1	EI	*KRT10*	Ex1	c.467G>A p.Arg156His	Typical EI, no additional features described
P16/F, 8	EI	*KRT10*	Ex1	c.467G>A p.Arg156His	Typical EI, no additional features described
P17/F, 32	EI	*KRT10*	Ex1	c.467G>T p.Arg156Leu	Typical EI, no additional features described
P18/F, 73	EI	*KRT10*	Ex1	c.482T>C p.Leu161Ser	Generalized ichthyosis with brown/grey scales and fissures, isolated blisters
P19/F, 1	EI	*KRT10*	Ex1	c.482T>C p.Leu161Ser	Typical EI, no additional features described
P20/M, 1	EI	*KRT10*	Ex6	**c.1345T>C p.Tyr449His**	Typical EI, no additional features described
P21-1/F, 58	CRIE	*KRT10*	In6	**c.1373+1G>C**	Erythroderma at birth, improvement during infancy. Age 57 years: Diagnosis of CRIE (development of white spots escaped attention up to this age). Development of patchy hyperpigmentation
P21-2/F, 22					Like the mother, the expression of CRIE is mild and resembles a mild to moderate type of CIE
P21-3/M, 25					Like the mother, the expression of CRIE is mild and resembles a mild to moderate type of CIE
P22/F, 6	CRIE	*KRT10*	In6	**c.1373+2T>C**	First clinical diagnosis was CIE. Age 4 years: First spots developed
P23/F, 35	CRIE	*KRT10*	In6	c.1374-1G>C p.Ser458Argfs*120	PPK, ectropion, severe mental delay, malposition of 4th toe, small height, facial dysmorphism, spasticity, agenesia of nipples, thick hairs, onychodystrophy. Histology: acanthosis, parakeratosis, cytolysis (suprabasal layers)
P24[1]/F, 6	CRIE	*KRT10*	Ex7	**c.1411_1412insA p.Gly471Glufs*110**	Collodion membrane and mild ectropion at birth. Development of a very inflammatory ichthyosis including alopecia totalis. Severe growth retardation. Joints partially blocked by constrictive skin. Age 2 years: first white spots were noted (shoulder). Age 6 years: multiple spots. Mutation *de novo*
P25[1]/F, 46	CRIE	*KRT10*	Ex7	**c.1544dupG p.Gly516Argfs*65**	PPK, slight mental delay, malposition of 4th toe, small height, facial dysmorphism, symblepharon. Histology: acanthosis, parakeratosis, cytolysis (suprabasal layers)
P26/F, 18	CRIE	*KRT10*	Ex7	**c.1544dupG p.Gly516Argfs*65**	Hypertrichosis. Histology: acanthosis, parakeratosis, cytolysis (suprabasal layers)

[1]Both next generation sequencing and Sanger sequencing were performed in these patients.

P: patient number; CRIE: congenital reticular ichthyosiform erythroderma; EI: epidermolytic ichthyosis; SEI: superficial epidermolytic ichthyosis; CIE: congenital ichthyosiform erythroderma; PPK: palmoplantar keratoderma.