somewhat high-risk because LI patients can show regional, individual, and familial variability in their disease phenotypes.[72] In LI families with *TGM1* mutations, successful prenatal DNA-base diagnosis and prenatal exclusion of LI have been reported.[73,74] Prenatal diagnosis by mutation analysis in lipoxygenase-3, 12(R)-lipoxygenase and ABCA12, etc. is theoretically available in LI and CIE families with previously identified mutations on a case by case basis.

Successful prenatal diagnosis for EI by fetal skin biopsy was reported in 1980s[75] and, at present, prenatal diagnosis by mutation analysis is feasible for EI in families whose causative mutations have been elucidated.[76,77]

CONCLUSION AND REMARKS

As I summarized above in this updated review, our knowledge on the molecular genetics and pathogenesis of ichthyosis has dramatically advanced in the last couple of decades. In addition, now we have several powerful tools for treatment of genetic disorders, for example, siRNA gene silencing technology, read-through compounds to read through nonsense mutations, and improved corrective gene transfer techniques. Fortunately, the skin is the most easily accessible organ for these novel treatment approaches. Thus, I am not pessimistic about development of novel, highly effective therapeutic methods in the near future, based on our knowledge on the pathomechanisms of various ichthyoses described here in the present review.

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Figure legends

Fig. 1 Major components of the skin barrier in the stratum corneum consist of intercellular lipid layers, cornified cell envelope and keratin/filaggrin degradation products. Figure modified from Ref. No. 1

Fig. 2 Clinical features of ichthyosis. (A) A HI patient harboring a homozygous *ABCA12* splice site mutation. Thick, plate-like scales are seen on the whole body. Figure modified from Ref. No. 11. (B) A CIE patient carrying compound heterozygous *ABCA12* nonsense and missense mutations. Fine, whitish scales are observed on erythrodermic skin. Figure modified from Ref. No. 42.

Table 1. Essential components of stratum cornuem barrier and causative molecules/genes for ichthyoses (modified from Ref. No. 1)

Stratum corneum Barrier components	Molecule	Gene (locus)	Mode of inheritance	Type of Mutations	Phenotype
Intercellular lipid layers	ABCA12	*ABCA12* (2q34)	AR	truncation/deletion (rarely missense)	HI
	ABCA12	*ABCA12* (2q34)	AR	missense/missense or missense/truncation	LI or CIE
	lipoxygenase-3	*ALOXE3* (17p13.1)	AR	missense/truncation	LI or CIE
	12*R*-lipoxygenase	*ALOX12B* (17p13.1)	AR	missense/truncation	LI or CIE
	Cytochrome P450 (CYP4F2 homolog)	*FLJ39501* (19P12)	AR	missense/truncation	LI
	NIPAL4	*NIPAL4* (5q33)	AR	missense/truncation	CIE or LI
	Steroid sulfatase	*STS* (Xp22.32)	X-LR	mostly large deletion	RXLI
Cornified cell envelope	TGase 1	*TGM1* (14q11.2)	AR	missense/truncation / deletion/insertion	LI or CIE
Keratin network and keratohyalin granules	keratin 1	*KRT1* (12q12-q13)	AD	missense	EI
	keratin 10	*KRT10* (17q21)	AD (rarely AR)	missense (rarely nonsense)	EI
	keratin 2	*KRT2* (12q11-q13)	AD	missense	SEI
	Filaggrin (profilaggrin)	*FLG* (1q21.3)	ASD	truncation	IV

AD, autosomal dominant; AR, autosomal recessive; ASD, autosomal semidominant; X-LR, X-linked recessive CIE, congenital ichthyosiform erythroderma; EI, epidermolytic ichthyosis; HI, harlequin ichthyosis; IV, ichthyosis vulgaris; LI, lamellar ichthyosis; RXLI, recessive X-linked ichthyosis; SEI, superficial epidermolytic ichthyosis

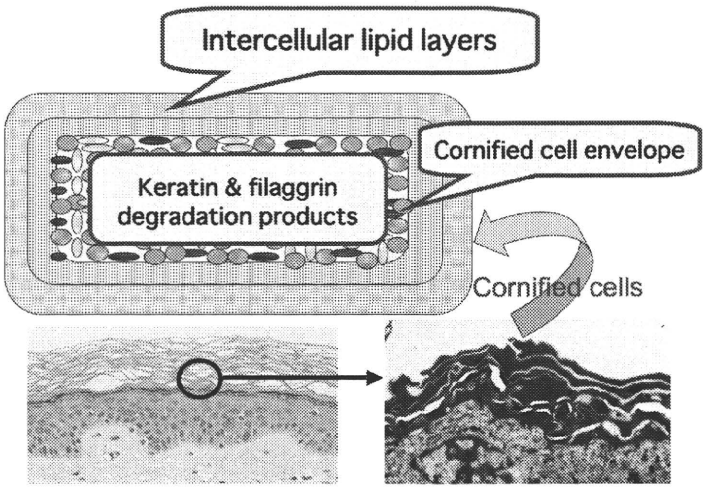

Figure 1.

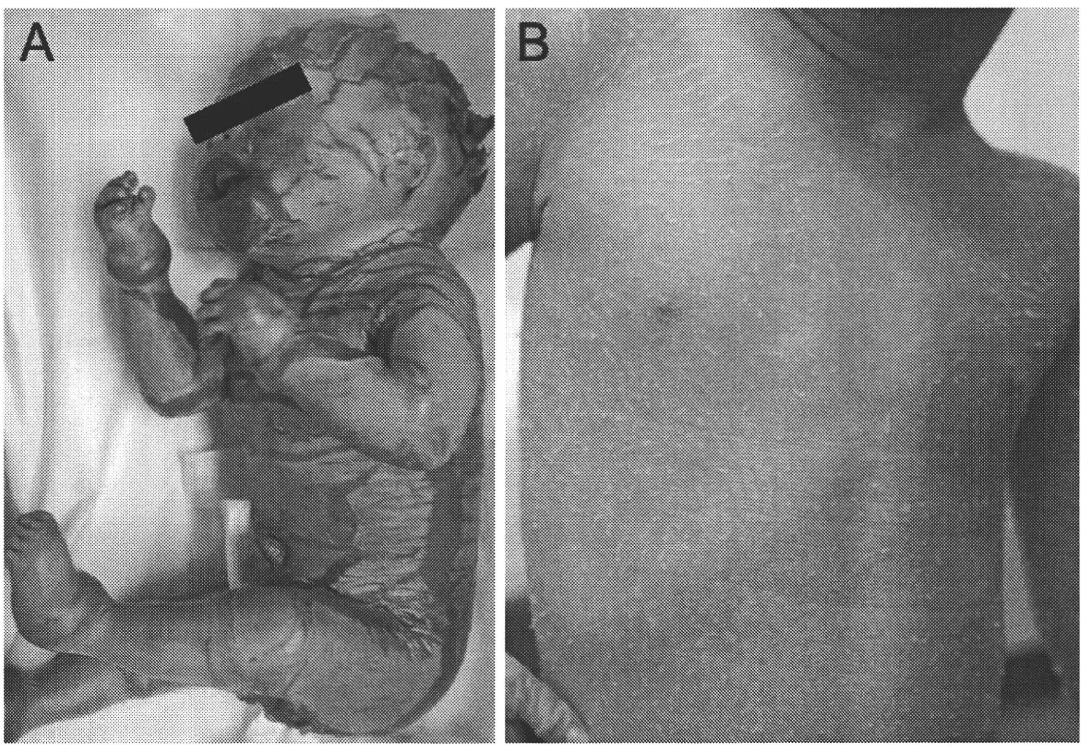

Figure 2.

British Journal of Dermatology

Review Article

Malignant Skin Tumours in Inherited Ichthyosis Patients

Running Head: Skin malignancies in inherited ichthyosis

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What's already known about this topic?

- There have been sporadic case reports of malignant skin tumours in congenital ichthyosis patients.
- The frequency of skin malignancies in ichthyosis patients is unknown.

What does this study add?

- Congenital ichthyosis patients, especially those with KID syndrome, congenital ichthyosiform erythroderma, lamellar ichthyosis and Netherton syndrome, can develop cutaneous squamous cell carcinoma at unusually young ages.