Supplementary information S1 (table) | **Human diseases of the epidermis**

Molecular target*	Disease	Phenotype
Gap junctions		
CX26	Keratitis ichthyosis deafness syndrome and hystrix-like ichthyosis deafness syndrome[1]	Vascularizing keratitis; progressive erythrokeratoderma; sensorineural hearing loss
	Vohwinkel's syndrome (keratoderma hereditaria mutilans)[2]	Keratoderma of palmoplantar surfaces; circumferential hyperkeratosis of digits leading to autoamputation; moderate sensorineural hearing loss
	Bart–Pumphrey syndrome[3]	Hyperkeratosis of knuckle pads; sensorineural hearing loss
CX30	Clouston syndrome (hidrotic ectodermal dysplasia)[4]	Palmoplantar hyperkeratosis; hair defects (partial to total alopecia); nail deformities
CX30.3, CX31	Erythrokeratodermia variabilis[5,6]	Local or diffuse hyperkeratosis; migratory erythematous patches
Adherens junctions		
P-cadherin (encoded by *CDH3*)	Hypotrichosis with juvenile macular dystrophy[7]	Hair loss; progressive macular degeneration and early blindness
	Ectodermal dysplasia, ectrodactyly, macular degeneration syndrome[8]	Hypotrichosis with partial adontia; absence deformities and syndactyly; atrophy of retinal pigment epithelium
Keratin intermediate filaments		
K4, K13	White sponge nevus[9,10]	Spongy white plaques, often on buccal mucosa
K9	Epidermolytic palmoplantar keratoderma[11]	Epidermolysis and hyperkeratosis of palms and soles
K6, K16, K17	Pachyonychia congenita[12,13]	Painful blisters on hands and feet; thickened nails; hyperkeratosis of hair follicles; leukokeratosis of oral mucosa
K2e	Ichthyosis bullosa of Siemens[14,15]	Bullous ichthyosis without erythroderma; epidermolysis limited to upper suprabasal layers
K1, K10	Bullous congenital ichthyosis erythroderma (epidermolytic hyperkeratosis)[16–18]	Generalized erythema; erosions and blisters owing to fragility of suprabasal keratinocytes
K5, K14	Epidermolysis bullosa simplex[19]	Skin blistering from fragility of basal keratinocytes
Desmosomes		
DSG1	Bullous impetigo[20]	Epidermal blisters at the granular layer caused by a bacterial protease
	Staphylococcal scalded skin syndrome[20]	
	Pemphigus foliaceus[21]	Epidermal blisters at the granular layer caused by autoantibodies
DSG3	Pemphigus vulgaris[22]	Epidermal blisters at the basal–suprabasal cell interface caused by autoantibodies
DSG4	Hypotrichosis[23]	Sparse, fragile hair with abnormal hair follicles; epidermal hyperproliferation
DSC3	Hypotrichosis with skin vesicles[24]	Sparse, fragile hair with normal hair follicles; recurrent skin vesicles
DSC2	Arrhythmogenic right ventricular cardiomyopathy with mild palmoplantar keratoderma and woolly hair[25]	Ventricular arrhythmias with fibro-fatty replacement of heart tissue; thickening of palms and soles; tightly coiled hair
DP, DSG1	Striate palmoplantar keratoderma[26–28]	Linear and focal hyperkeratosis of palms and soles
DP	Carvajal syndrome[29]	Epidermolytic palmoplantar keratoderma with woolly hair and dilated cardiomyopathy
	Lethal acantholytic epidermolysis bullosa[30]	Acantholysis and shedding of skin at birth, leading to early death
PKP1	Ectodermal dysplasia-skin fragility syndrome[31]	Skin fragility; plantar keratoderma; nail dystrophy; alopecia
PG	Naxos disease[32]	Woolly hair; palmoplantar keratoderma; arrhythmogenic right ventricular cardiomyopathy
	Lethal congenital epidermolysis bullosa[33]	Lethal epidermal blistering at birth
Hemidesmosomes		
Laminins, integrins, BPAG2	Junctional epidermolysis bullosa[34–37]	Generalized blistering at dermal–epidermal junction due to either congenital mutation or acquired autoantibodies
BPAG1e	Epidermolysis bullosa simplex[38]	Trauma-induced epidermal blisters and episodic limb numbness
Plectin	Epidermolysis bullosa simplex with muscular dystrophy[55]	Epidermal bullous disease coupled with a severe, slowly progressive, muscle atrophy
BPAG2	Bullous pemphigoid[39]	Fluid-filled subepidermal blisters with deroofing of epidermis caused by autoantibodies

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Molecular target*	Disease	Phenotype
Stratum corneum		
ABCA12 (lipid transport)	Harlequin ichthyosis[40,41]	Hard, thickened skin with fissures
Filaggrin	Ichthyosis vulgaris[42]	Dry skin; mild hyperkeratosis
CDSN	Hypotrichosis simplex of scalp[43]	Childhood-onset loss of hair
	Generalized peeling skin syndrome[44]	Peeling of the skin and itching
SPINK5 (also known as LEKT1; serine protease inhibitor)	Netherton syndrome[45]	Exfoliative erythroderma; hair abnormalities; atopic manifestations
TGase 1	Lamellar ichthyosis[46–48]	Newborns covered with colloid membrane that is later shed; erythema with white scales; hyperkeratosis of palms and soles
Loricrin	Vohwinkel's syndrome (keratoderma hereditaria mutilans)[49]	Keratoderma of palmoplantar surfaces; circumferential hyperkeratosis of digits leading to autoamputation; moderate sensorineural hearing loss
	Progressive symmetric erythrokeratodermia[50]	Hyperpigmented, hyperkeratotic plaques with symmetrical growth
Other		
ATP2C1 (calcium pump)	Hailey–Hailey disease[51]	Outbreaks of rashes and blisters, usually in skin folds
ATP2A2 (calcium pump)	Darier's disease[52]	Acantholysis; abnormal keratinization; greasy, hyperkeratotic papules
Collagen VII	Dystrophic epidermolysis bullosa[53]	Severe blistering with atrophic scarring
Kindlin 1	Kindler syndrome[54]	Skin atrophy with blistering at dermal–epidermal junction

ABCA12, ATP-binding cassette, sub-family A, member 12; ATP2A2, sarcoplasmic/endoplasmic reticulum calcium ATPase 2; ATP2C1, calcium-transporting ATPase type 2C member 1; BPAG, bullous pemphigoid antigen; *CDH3*, cadherin 3; CDSN, corneodesmosin; CX, connexin; DP, desmoplakin; DSC, desmocollin; DSG, desmoglein; K, keratin; PG, plakoglobin; PKP1, plakophilin 1; TGase 1, transglutaminase 1. *Listed molecular targets are affected by gene mutation in these diseases unless otherwise specified.

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