SCIENTIFIC UNDERSTANDING OF THE STRATUM CORNEUM:PHYSIOLOGY, FUNCTION AND EFFECT ON SKIN APPEARANCE

Percorso di “Benessere, Make-up e Inestetismi da Terapia”

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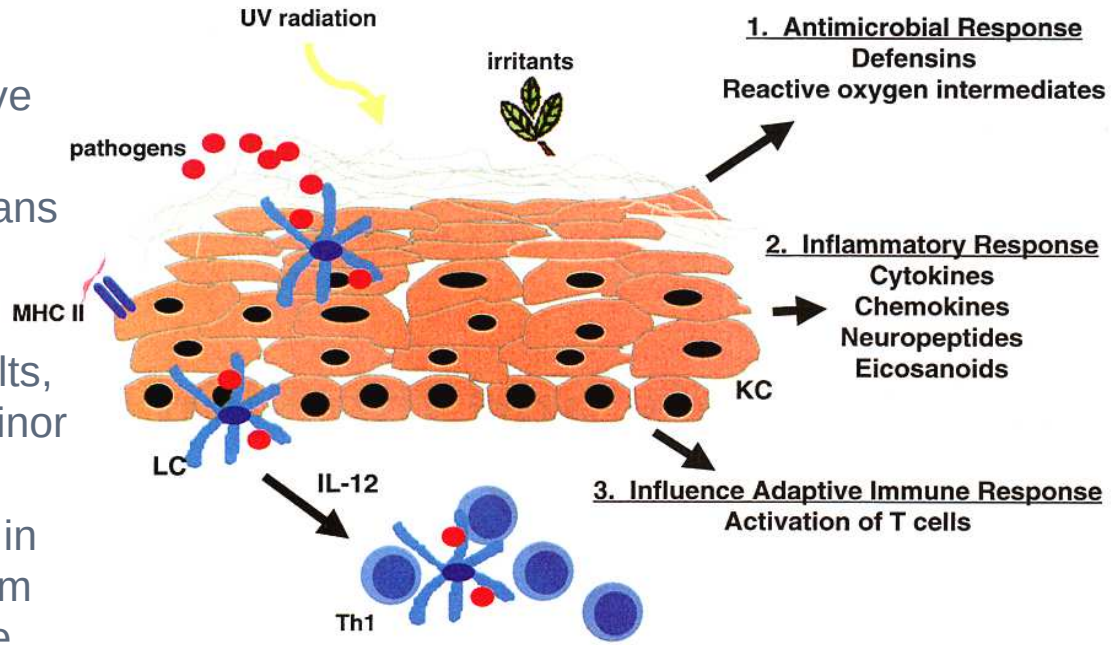
SKIN PHYSIOLOGY - MANY FUNCTIONS

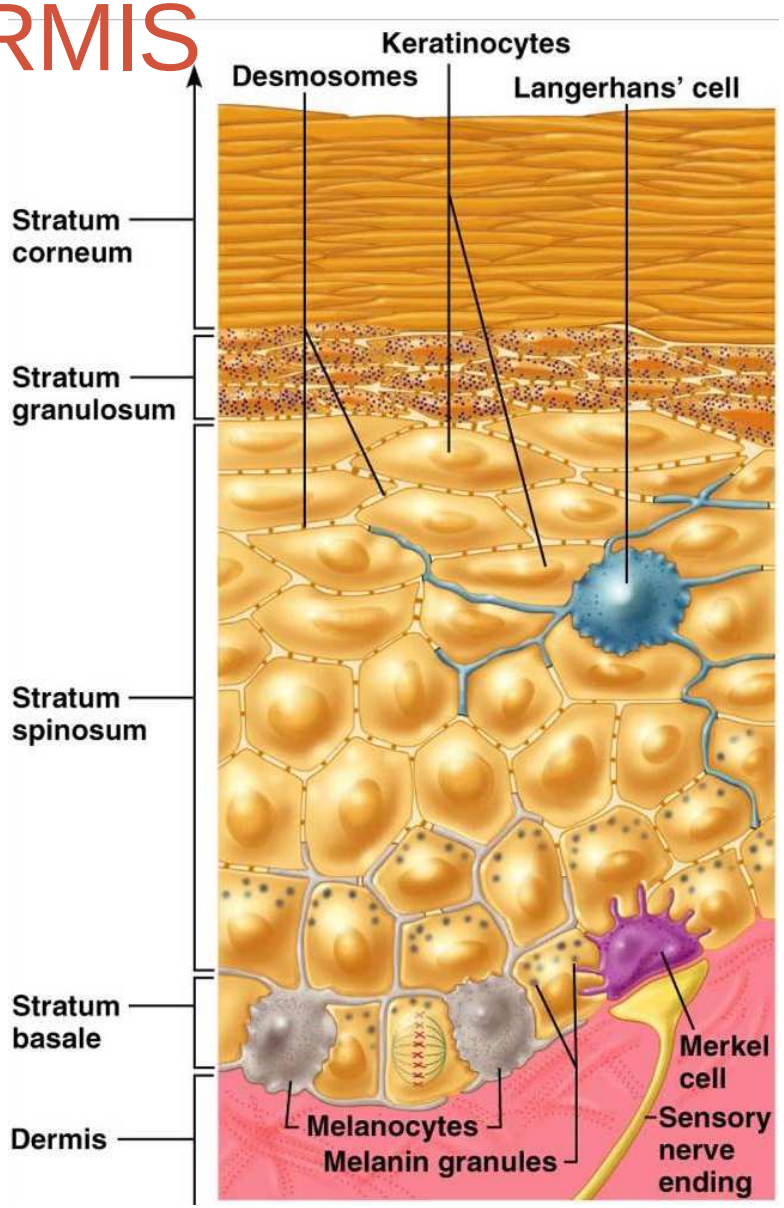
- regulation of body temperature – insulator, radiator
- protection – a physical barrier and for water conservation
- sensation - varied sensory nerve endings
- communication – to other humans by signals/expressions and by touch
- excretion – in sweat = H2O, salts, small organic compounds (a minor contribution to excretion)
- immunity – certain phagocytes in the epidermis are important from the immune system for defense
- the dermis is a significant blood reservoir
- synthesis of Vitamin D – for calcium absorption



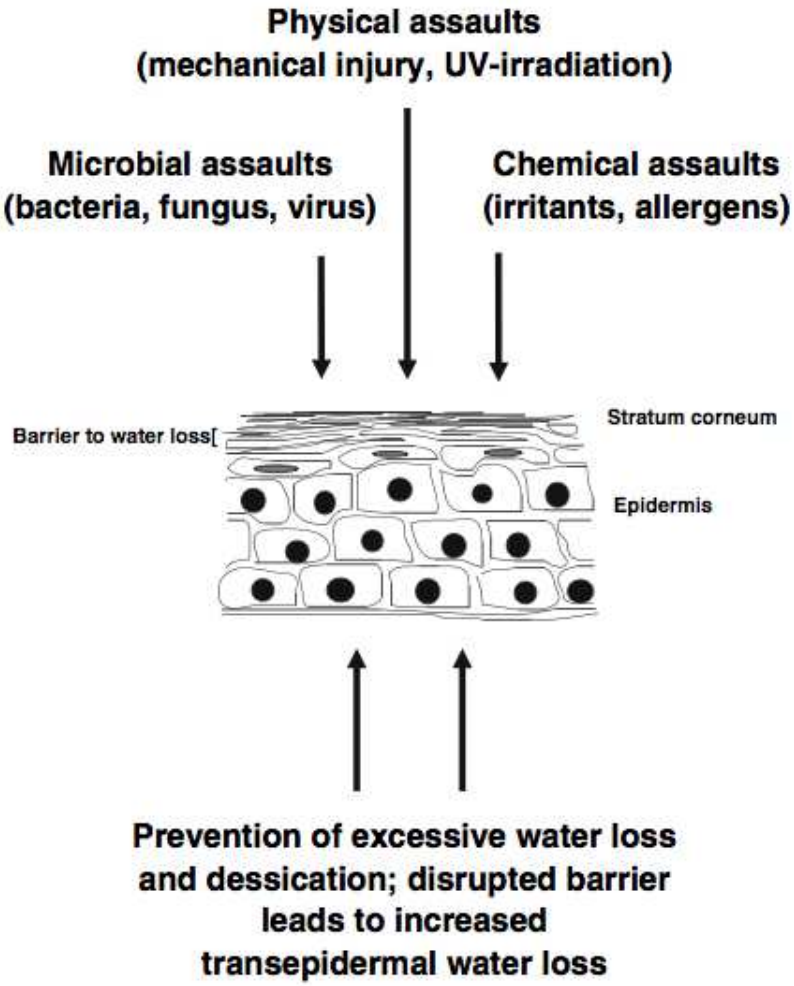
THE EPIDERMIS

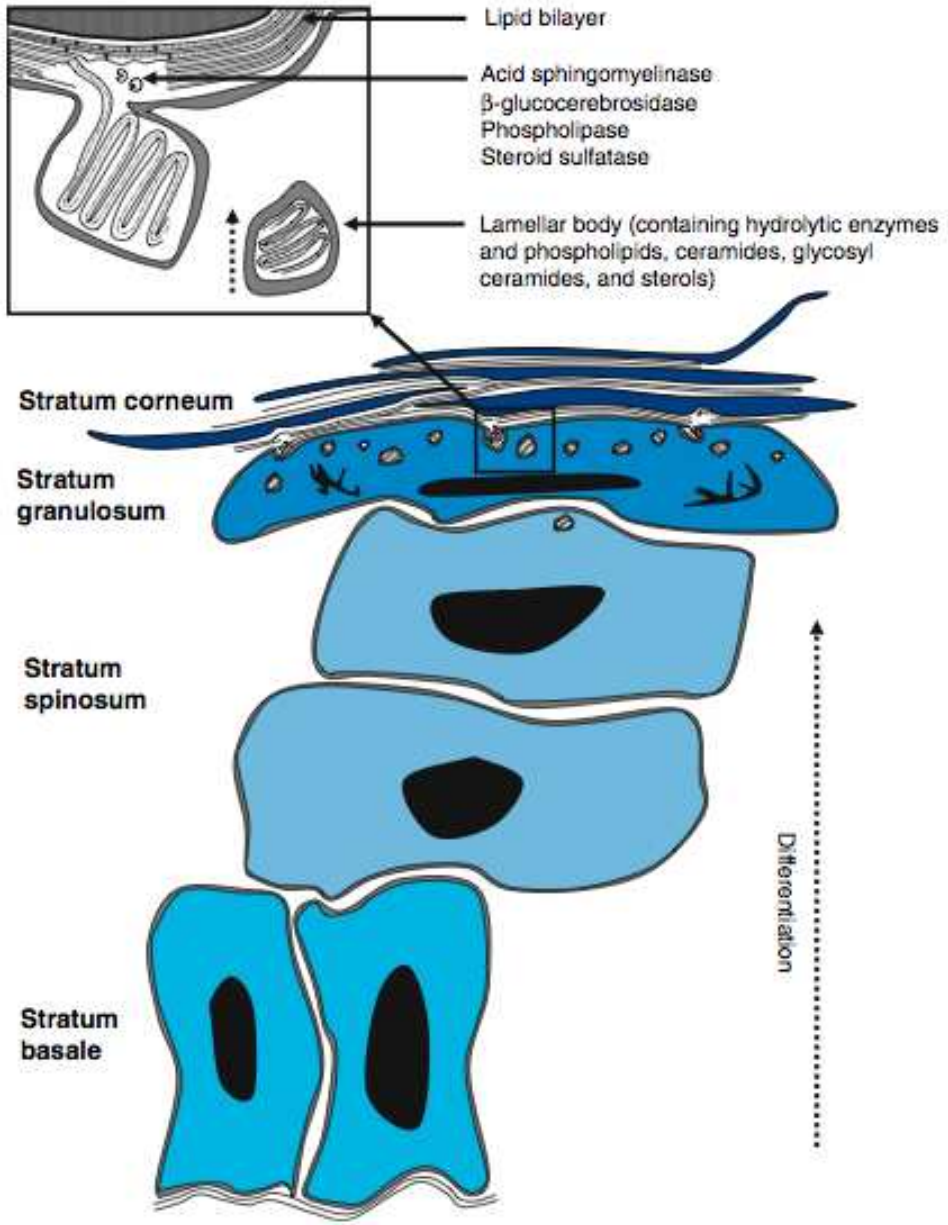
- Stratified Squamous Epithelium

- 4 cell types
  - Keratinocytes - 90%
    - filled with keratin (protein)
    - waterproof barrier
  - Melanocytes - 8%
    - produce melanin (pigment)
    - pass melanin to keratinocytes
  - Langerhans cells
    - phagocytes (from immune system)
    - easily damaged by UV light
  - Merkel cells
    - in deepest layer of hairless skin
    - sensory transduction - touch

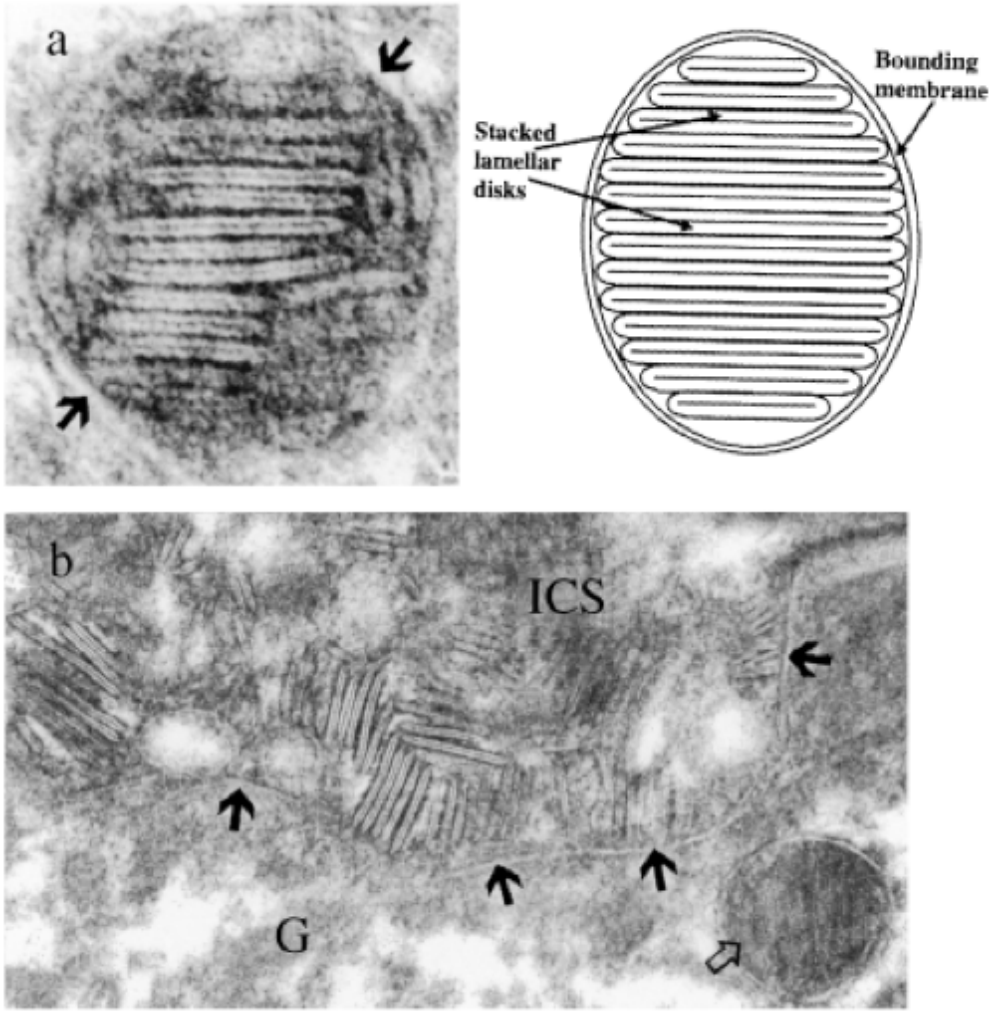


FUNCTIONS OF THE STRATUM CORNEUM

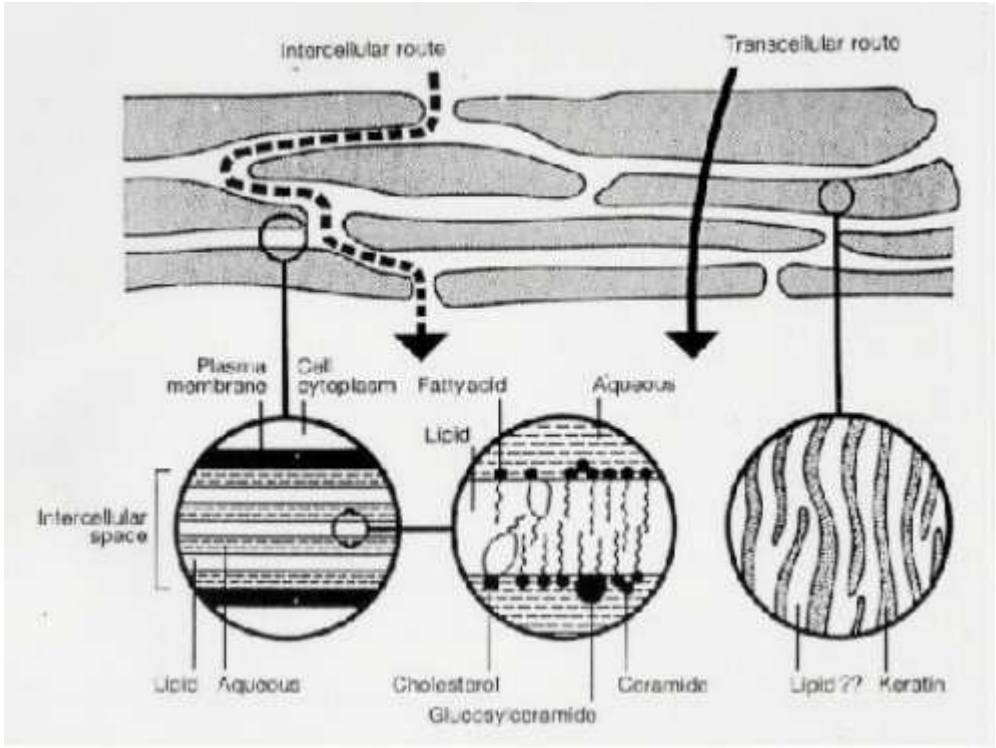


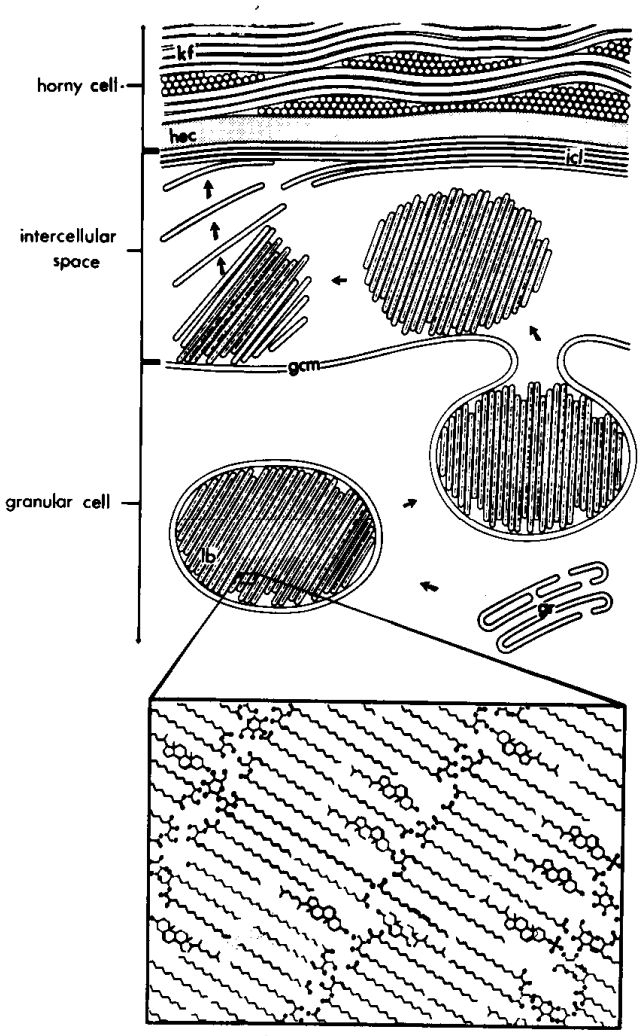


LAMELLAR BODIES

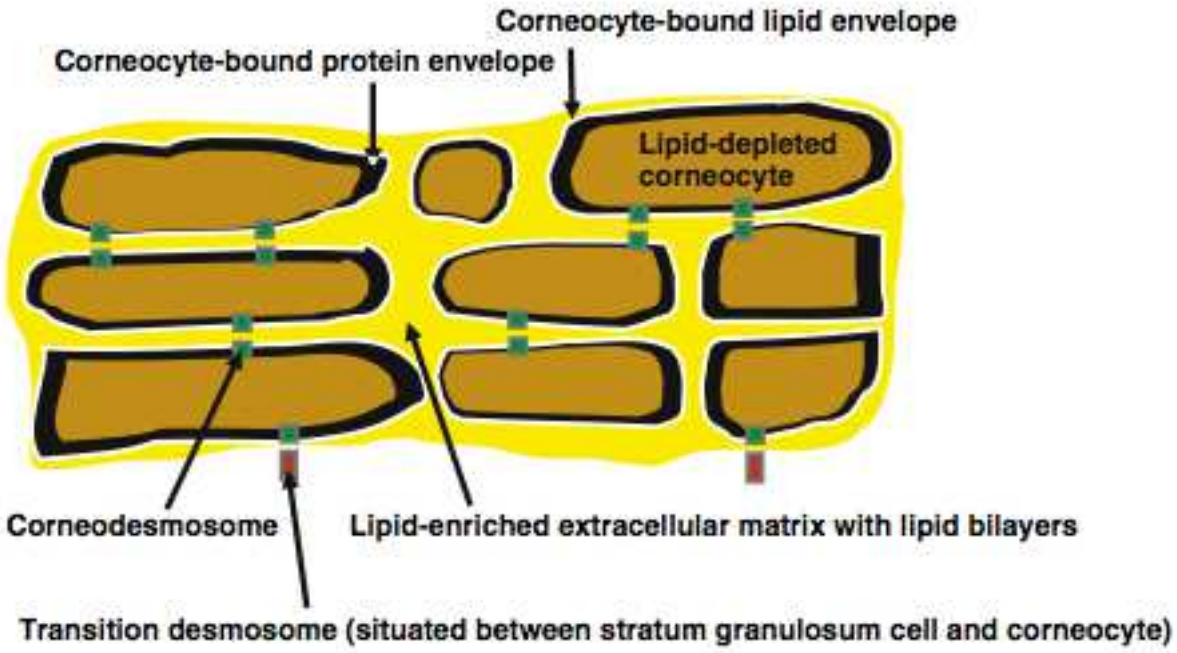


STRATUM CORNEUM INTERCELLULAR LIPIDS





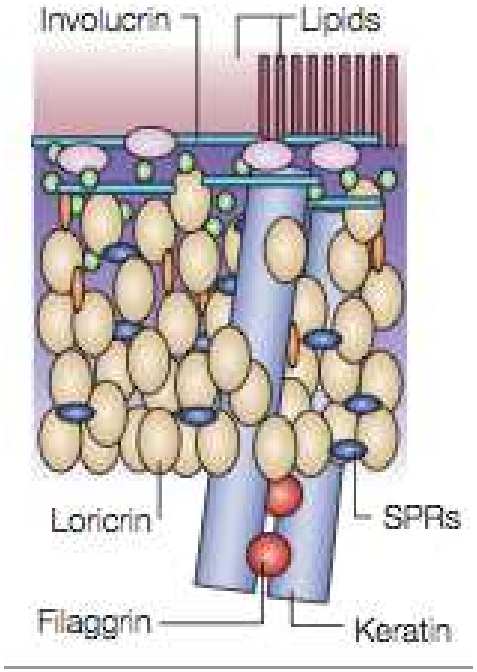
CORNEOCYTES



Proksh E et al, Exp Derm 2008

CORNEOCYTE ENVELOPE

- Protein envelope
  - Envoplakin, involucrin, small proline rich (SPR), loricrin
  - Formed by transglutaminases 1-3
  - Two subtypes
    - Fragile (Cef) rough in lower s.c. layers
    - Rigid (Cer) flat in superficial s.c.
- Lipid envelope
  - Plasma membrane-like structures
  - Interdigitate with intercellular lipid lamellae



QUALITATIVE CHANGES IN SKIN LIPID COMPOSITION DURING STRATUM CORNEUM MATURATION

	basal	granular	corneum
phospholipids	44.5	25.3	4.9 -
colest. sulphate	2.4	5.5	1.5 -
glucosylceramides	3.5	5.8	tracce
ceramides	3.8	8.8	18.1 ++
sterols	11.2	11.5	14
FFA	7	9.2	19.3 ++
triglycerides	12.4	24.7	25.2 +
Wax esters	5.3	4.7	5.4
squalene	4.9	4.6	4.8
n-alkans	3.9	3.8	6.1

ATOPIC DERMATITIS

Table 1. Human studies on SC lipids in patients with AD

Patients	Collection of SC	Lipid analysis	Results	Reference
47 AD patients with lesional skin from 28 and non-lesional skin from 19	Cyanoacrylate strip	HPTLC	Reduced total ceramides Reduced ceramides 1 and 3 Increased cholesterol	43
35 AD patients with both lesional and non-lesional skin	Cyanoacrylate on a glass slide	TLC	Reduced total ceramides Reduced ceramide 1	44
6 AD patients with non-lesional skin	By rinsing with ethanol	HPTLC	Reduced ceramide 1	45
10 AD patients with non-lesional skin	Cyanoacrylate strip	HPTLC	Reduced ceramides 1 and 3	46

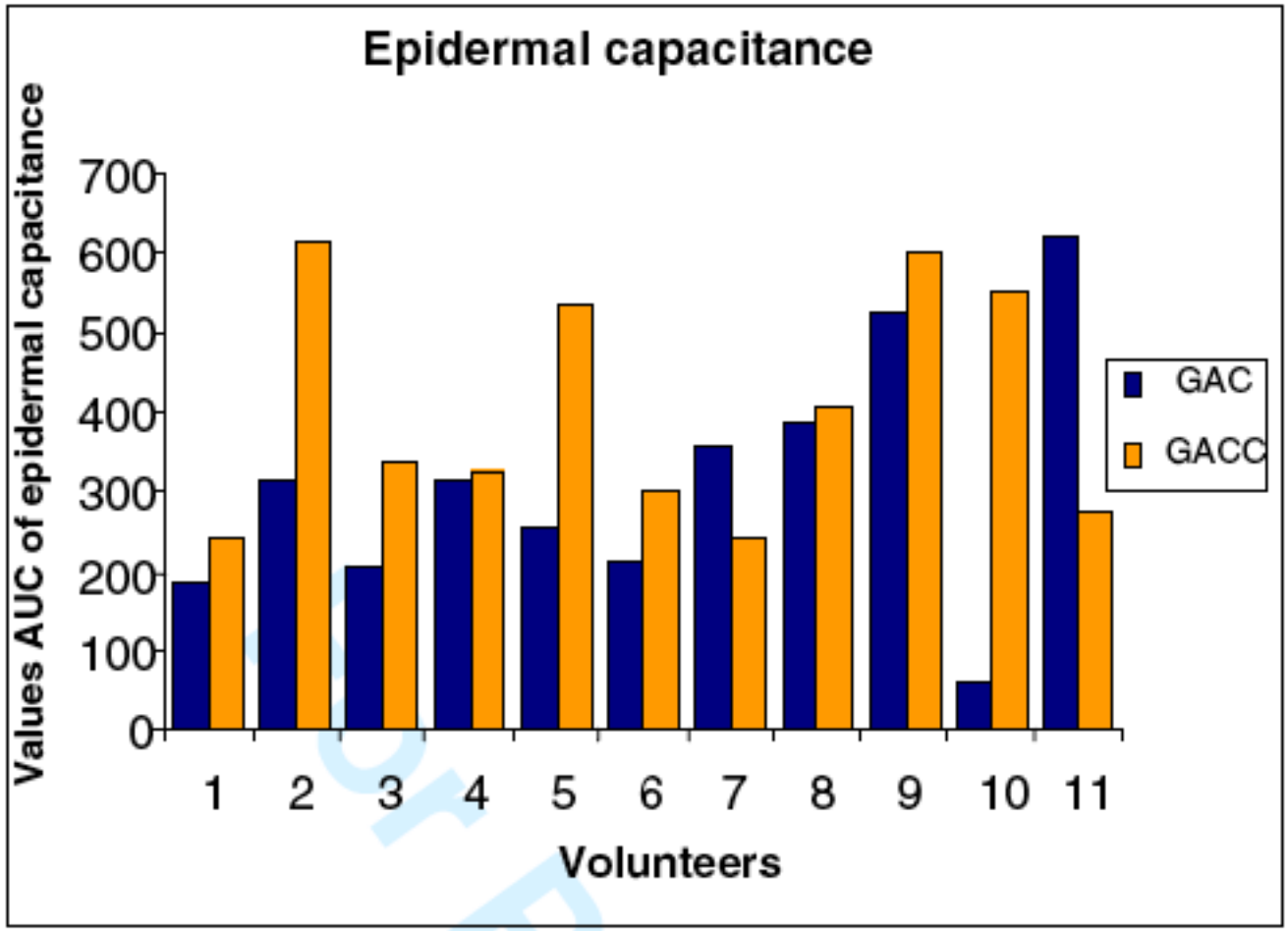
AD, atopic dermatitis; HPTLC, high-performance thin-layer chromatography; TLC, thin-layer chromatography.

CERAMIDES IN INVOLVED AND UNIVOLVED ATOPIC SKIN

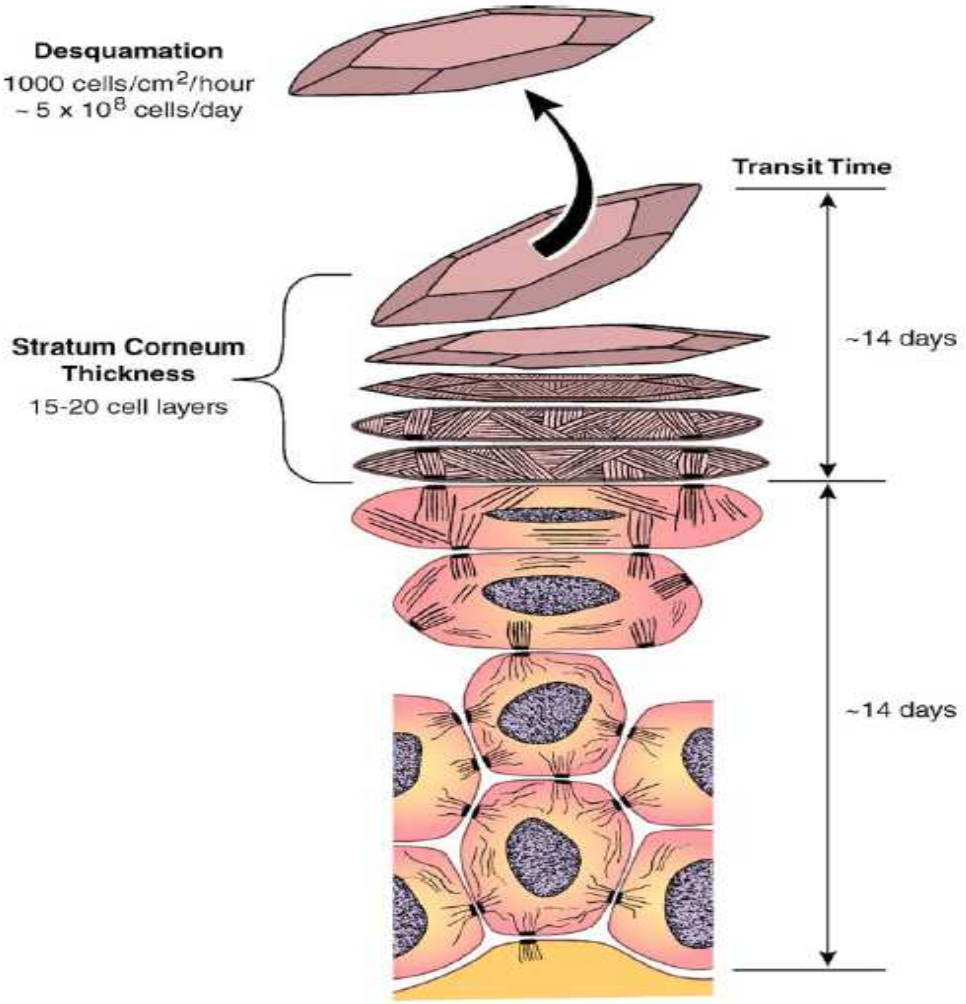
	control	normal skin	xerosis
total ceramides	31	21	20
ceramide 1	2.7	1.5	1.1
ceramide 2	6.5	4.3	5.0
ceramide 3	6.2	4.2	3.6
ceramide 4 and 5	8.2	5.9	5.1
ceramide 6	7.6	5.9	5.1

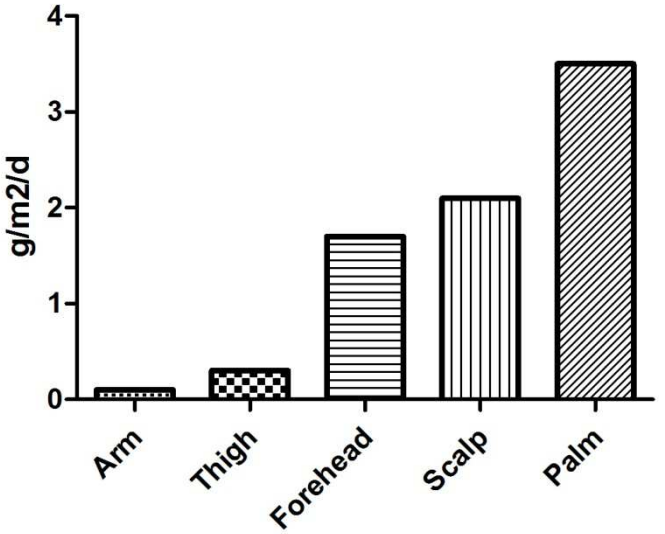
Imokawa et al. 1991

CERAMIDES AND SKIN HYDRATION



DESQUAMATION





DESQUAMATION

- **Degradation of corneodesmosomes**
  - Induced by several enzymes
- **Controlled by pH and water levels**
  - Dependent on filaggrin and NMFs

ENZYMES CONTROLLING DESQUAMATION

- Stratum Corneum Chymotryptic Enzyme (SCCE, KLK7)
- Stratum Corneum tryptic Enzyme (SCTE, KLK5)
  - Neutral pH
- Cathepsin family
  - Group of 3 enzymes working in superficial layers at low pH

Sulphatases	Steroid sulphatase	
Glycosidases	Heparanase 1	
Serine proteases	Stratum corneum chymotryptic-like enzyme	(SCCE/KLK7)
	Stratum corneum tryptic-like enzyme	(SCTE/KLK5)
Cysteine proteases	Stratum corneum thiol protease	(SCTP)
	Stratum corneum cathepsin E-like enzyme	(SCCEE)
Aspartic proteases	Stratum corneum cathepsin D-like enzyme	(SCCDE)

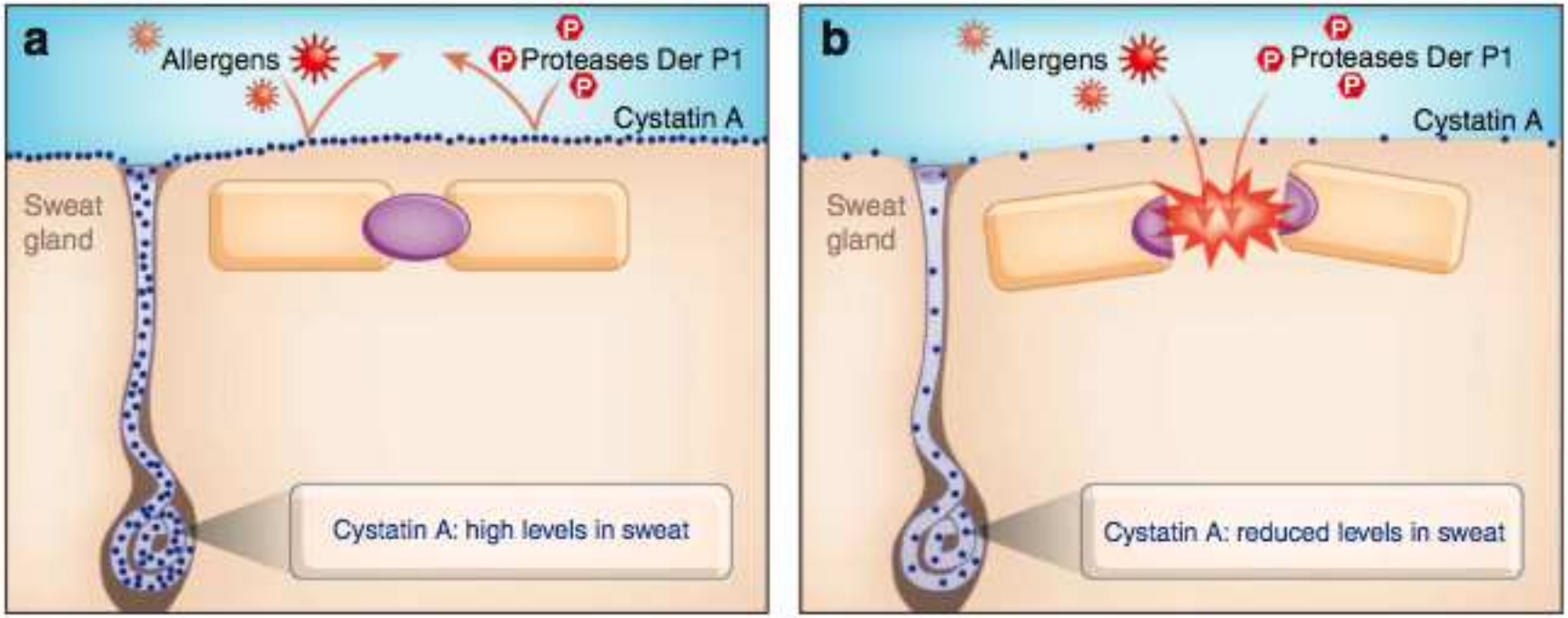
PROTEASES IN AD

Serine protease	Enzyme activity		
	Healthy	Nonlesional	Lesional
SC tryptase-like enzyme	0·71 ± 0·29	0·87 ± 0·32	39·41 ± 10·77*
Plasmin	0·53 ± 0·11	1·22 ± 0·34	36·38 ± 10·42*
Urokinase	0·40 ± 0·13	0·46 ± 0·12	3·25 ± 0·75*
Leucocyte elastase	0·01 ± 0·01	0·16 ± 0·16	3·13 ± 1·45*
Trypsin-like kallikreins (KLK5)	1·40 ± 0·27	1·26 ± 0·25	7·29 ± 1·48**
Chymotrypsin-like kallikreins (KLK7)	0·84 ± 0·18	0·42 ± 0·09	1·62 ± 0·28*

SC, stratum corneum. *$P < 0·05$; **$P < 0·01$.

Voegeli R et al, BJD, 2009

PROTEASE INHIBITORS PROTECT THE EPIDERMAL BARRIER FROM DEGRADATION



WATER IN THE STRATUM CORNEUM

- Filaggrin
- NMF
- Aquaporin-3
- Polar lipids

Reduction in the water content beyond a certain level will slow the desquamation process

FILAGGRIN

- Source of NMFs
- Synthesized from profilaggrin by a dephosphorilation step in the uppermost keratinocytes
- Subsequently is hydrolized to NMFs at the corneum-granulosum interface

NMFs

Constituent	% of total
Free amino acids	**58**
Serine	(26)
Glycine	(13)
Alanine	(10)
Arginine	(5)
Glutamic acid	(3)
Tyrosine	(1)
Pyrrolidone carboxylic acid	**17**
Salts	**15**
Sodium chloride	(7)
Sodium lactate	(7)
Potassium citrate	(1)
Urea	**10**
Sugars	**Trace**
Glucose	
Fructose	

NMFs

- Should be present in the s.c.
  - PCA (pyrrolidone carboxylic acid)
  - Urocanic acid
  - Aminoacids
  - Urea
  - A level of water too high or low will impair the activity of the enzymes involved in the production of NMF components
- High RH reduces the formation of NMF

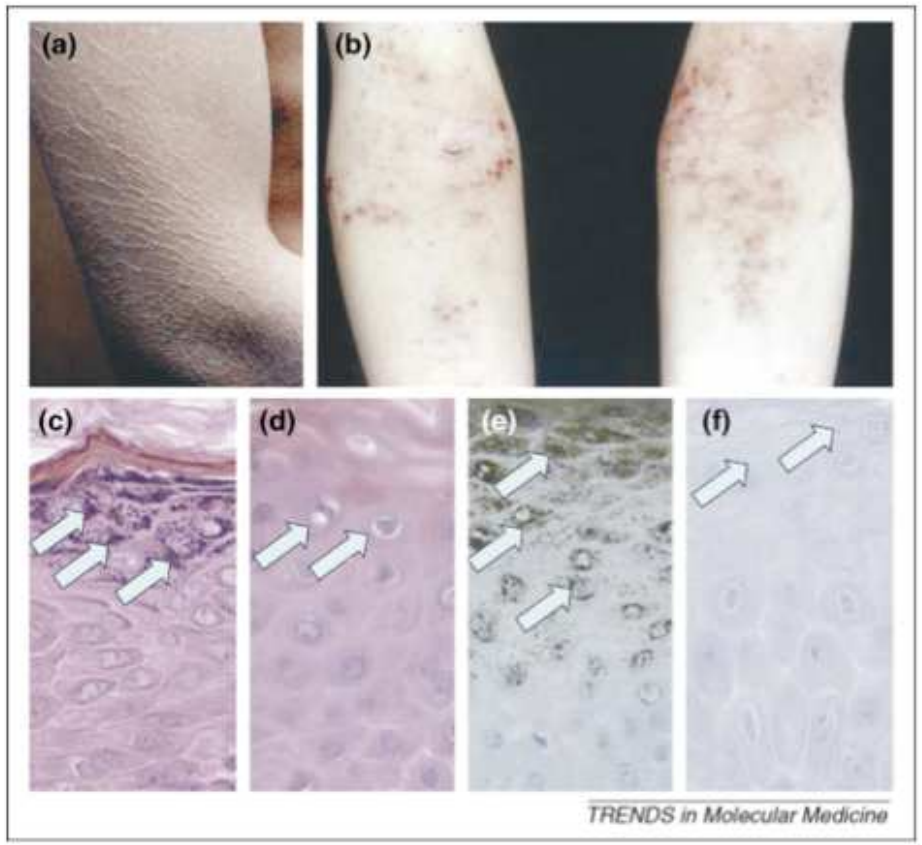
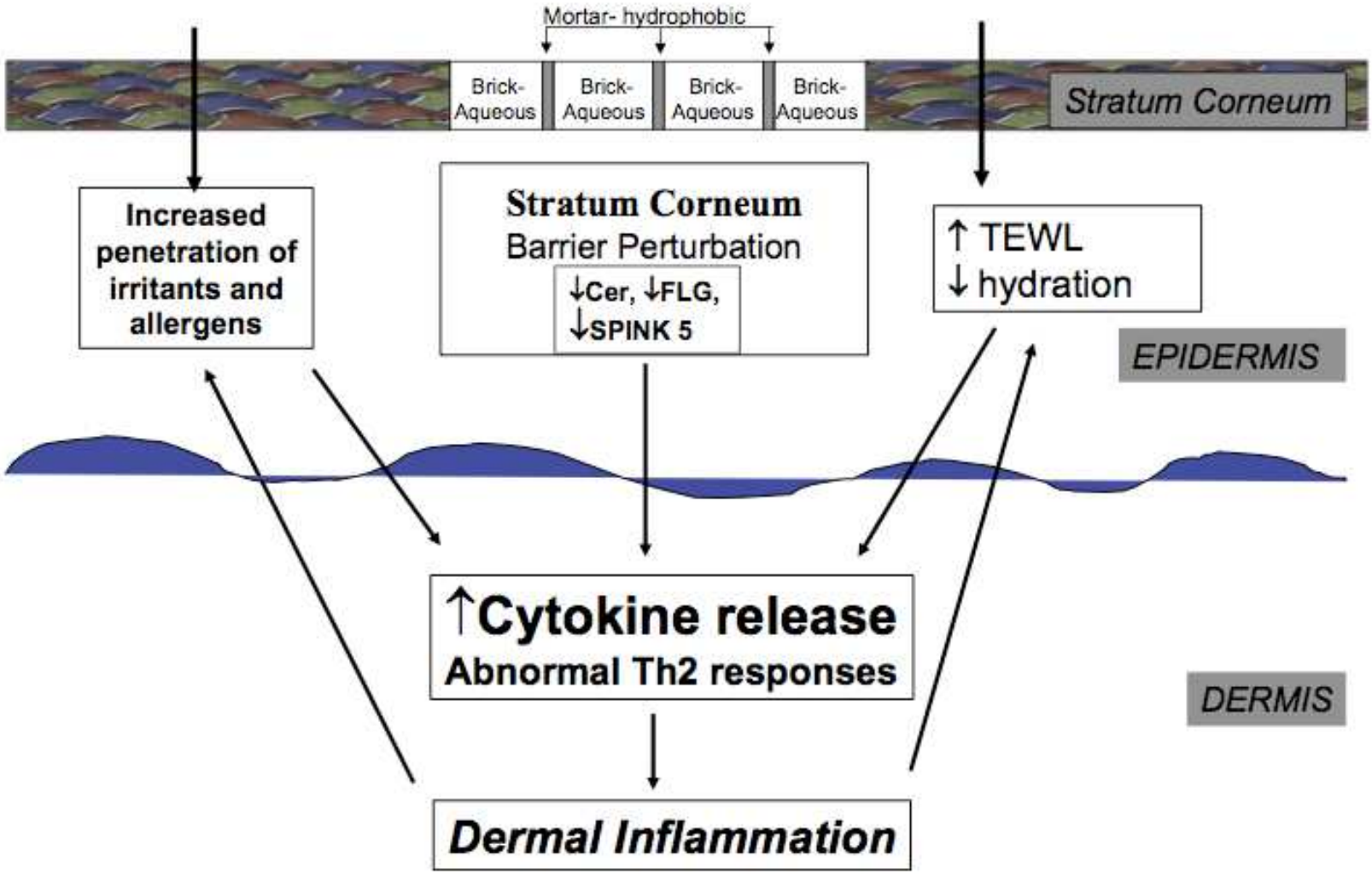


Figure 1. Clinical disorders associated with reduced profilaggrin expression in human skin. **(a)** IV with dry, scaly skin on the arm. **(b)** AD manifesting with erythema, erosions, inflammatory papules and lichenification on the antecubital fossae. **(c)** Histopathology of the upper epidermis in normal human skin. Note that the granular layer contains numerous dense aggregates known as keratohyalin granules (arrows). **(d)** In IV, no keratohyalin granules are present and the keratinocyte nuclei (arrows) appear to be degenerated. **(e)** Immunolabeling with a profilaggrin antibody in normal skin shows positive reactivity within the keratohyalin granules (arrows). **(f)** By contrast, in IV skin, owing to a homozygous nonsense mutation in the profilaggrin gene, there is a complete absence of profilaggrin immunoreactivity in the granular layer (arrows). Parts c–f adapted from [12].

ATOPIC DERMATITIS



SKIN BARRIER DYSFUNCTION IN AD

1. dry skin – increased transepidermal water loss

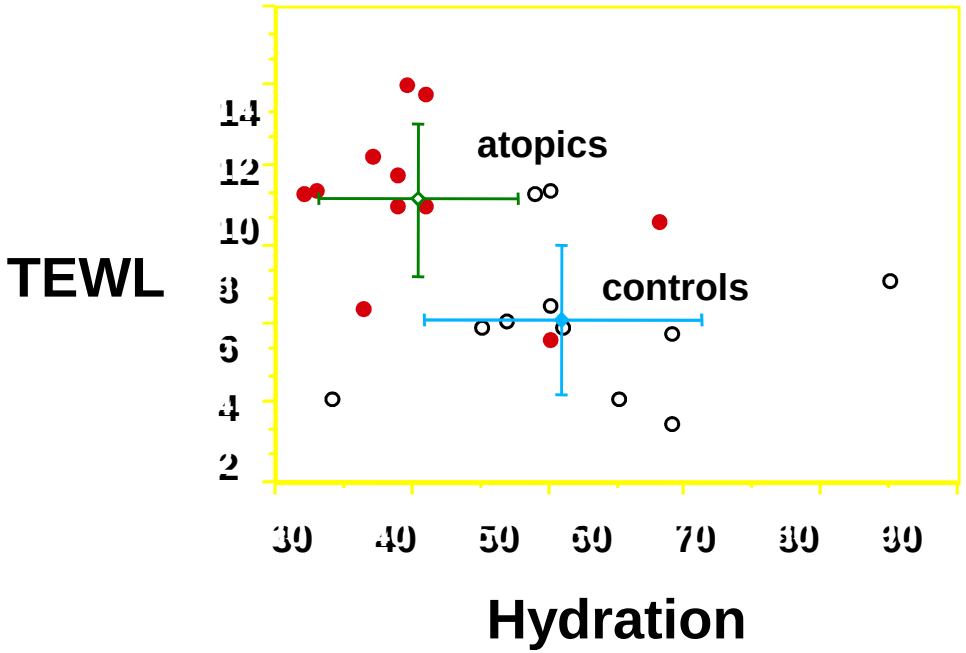
2. reduced content of ceramides and other lipids

3. changes in stratum corneum pH level

4. altered filaggrin profiles

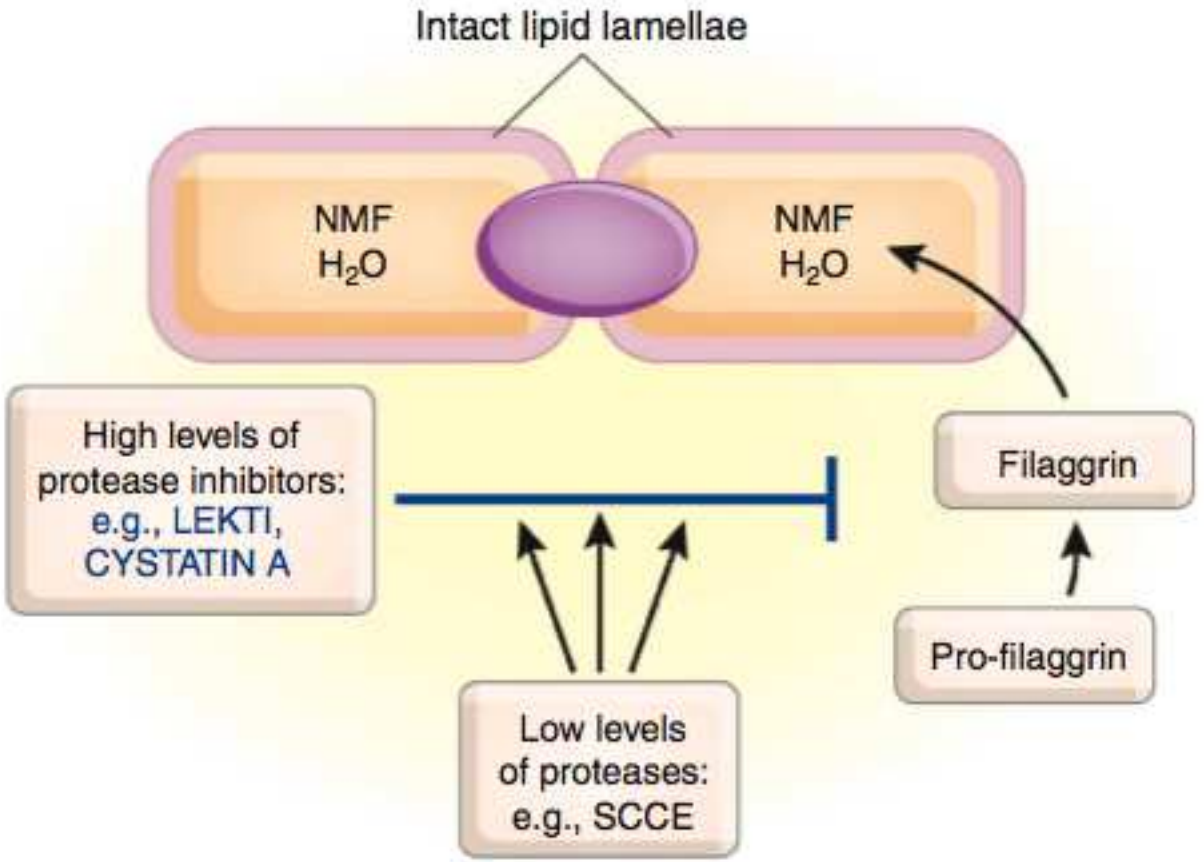
5. altered keratinocyte cytokine profile

BARRIER FUNCTION IN UNINVOLVED ATOPIC SKIN



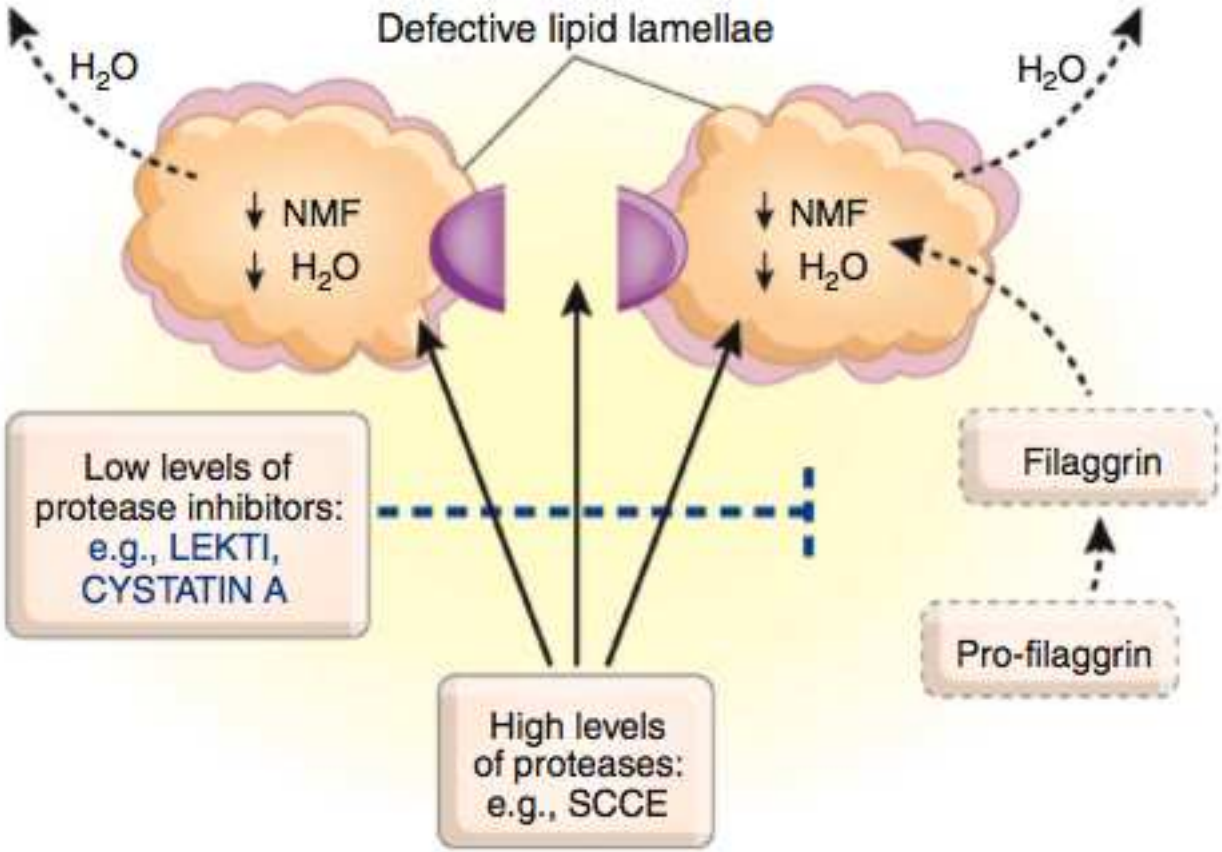
Berardesca et al, 1991

INTACT BARRIER FUNCTION

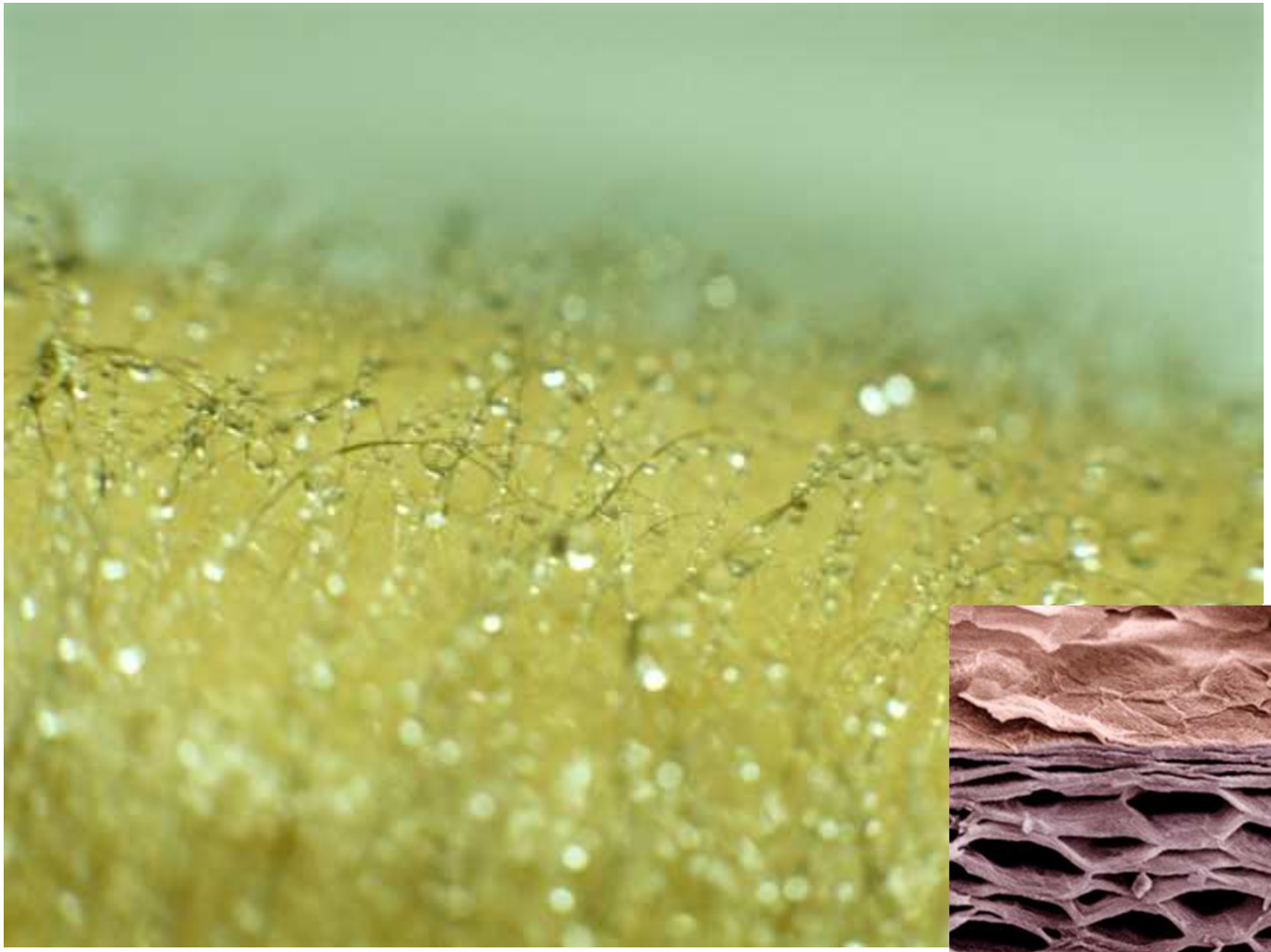


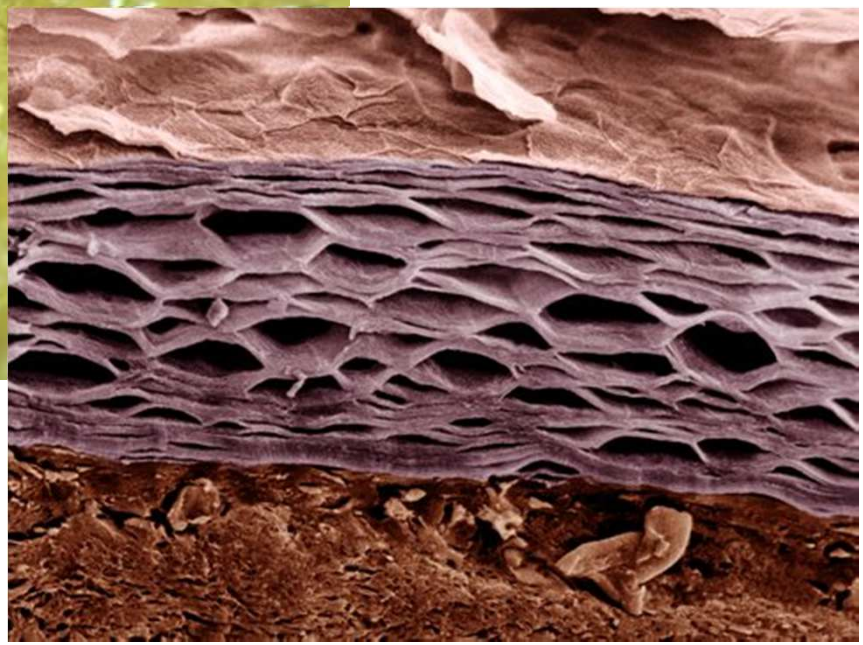
Cork M et al, JID 2009

DERANGED BARRIER FUNCTION

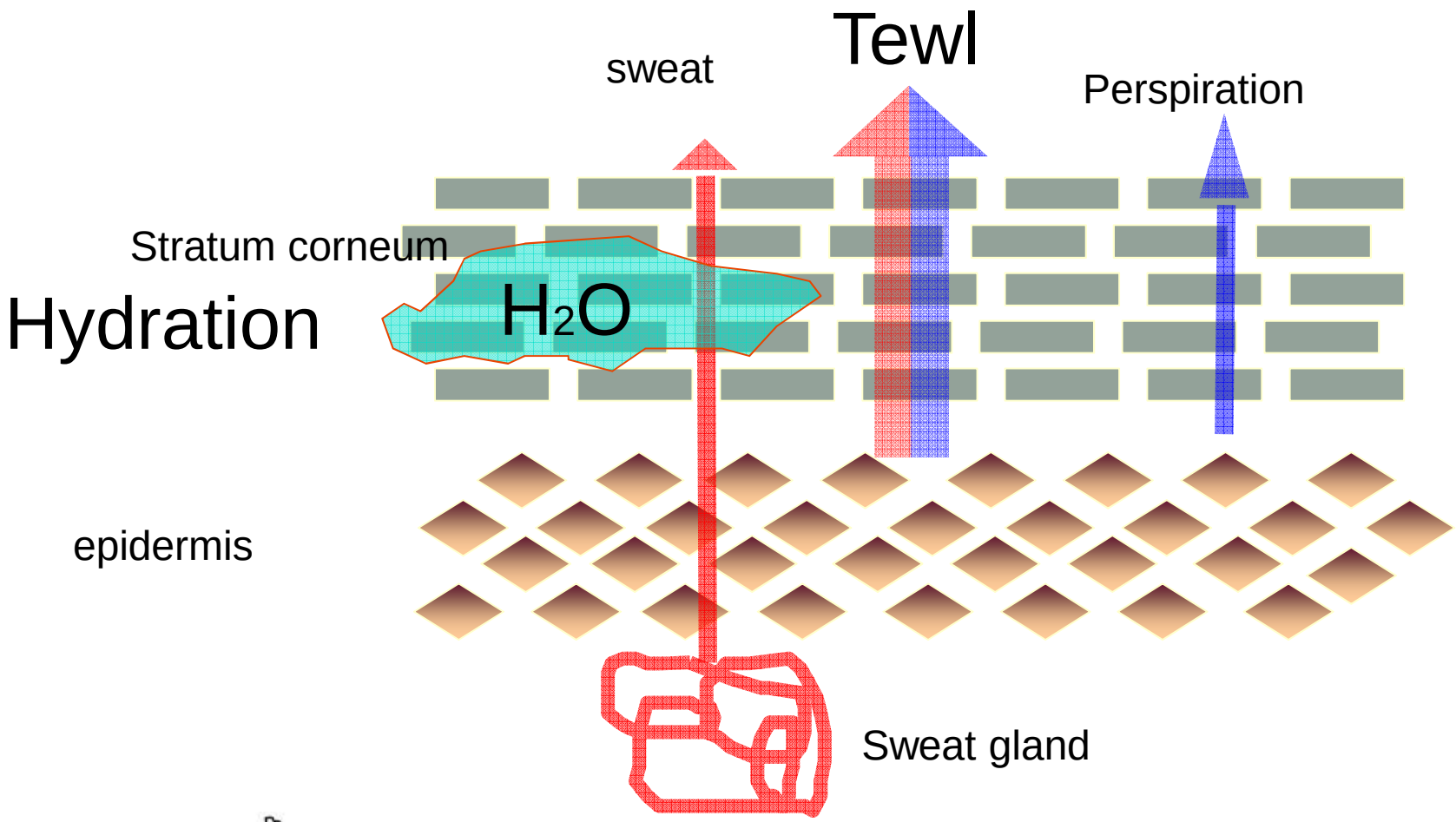


Cork M et al, JID 2009





TRANSEPIDERMAL WATER LOSS (TEWL) AND HYDRATION



FACTORS INFLUENCING DRY SKIN FORMATION

Roughness

Tightness

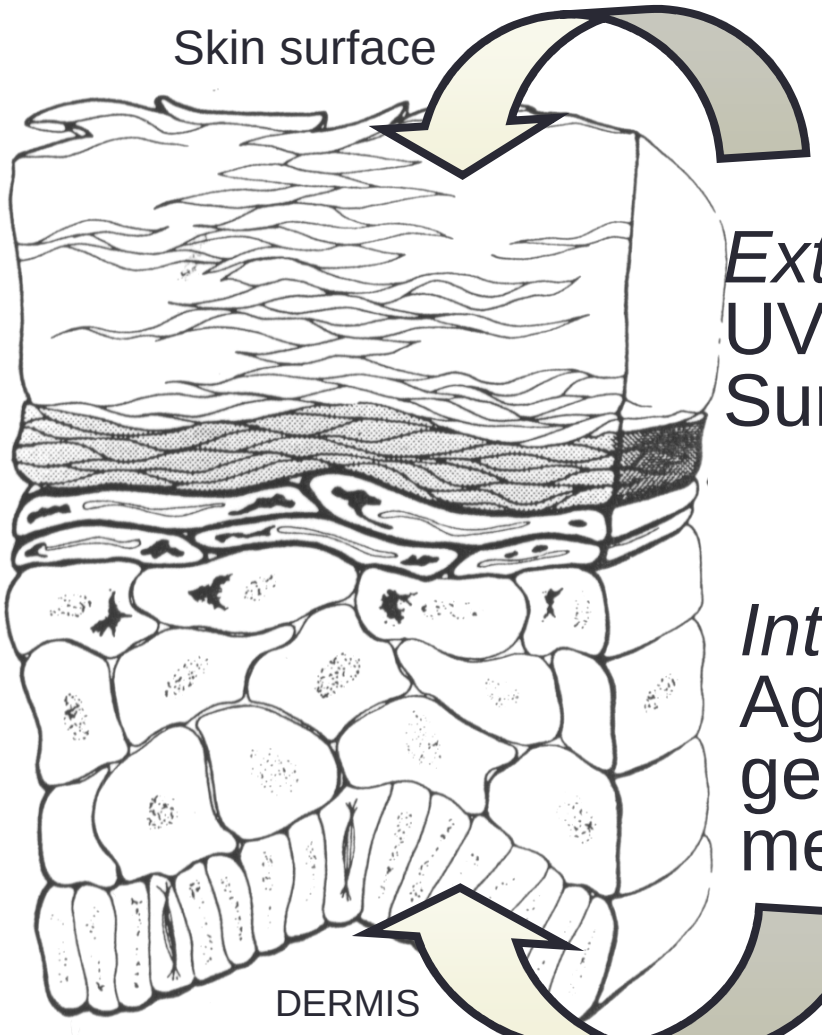
Chapping

Flaking

Itching

Cracking

Sore



Extrinsic Factors
UV, low RH/temp
Surfactants

Intrinsic Factors
Age, diet, stress, genetics, menopause

DRY SKIN FORMATION AND THE SC

- Many factors, both intrinsic & extrinsic can initiate dry skin formation
- Dry skin formation invariably begins with the:
  - Generation of a barrier perturbation
  - Persistence of a barrier perturbation
- Barrier perturbation can lead to hyperproliferation and inferior keratinocyte differentiation
  - Defective barrier formation
  - Development of a vicious cycle of deterioration

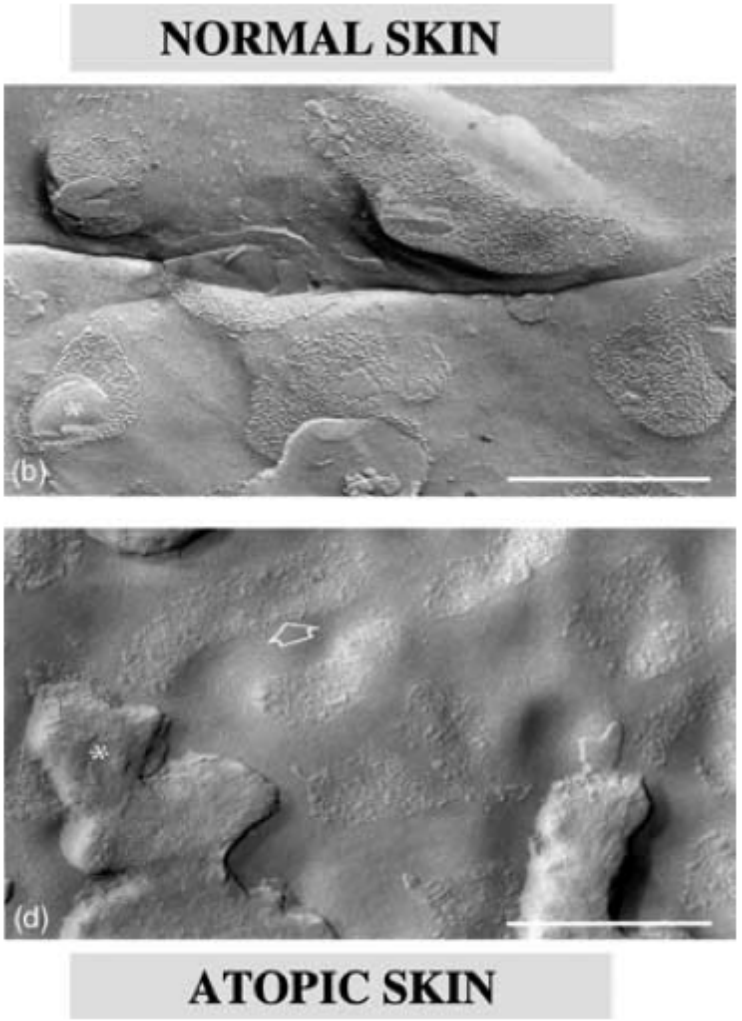
SC DRYNESS: WHAT IS OCCURRING?

- Disruption of stratum corneum lipids
- Decreased water content in stratum corneum
- Abnormal desquamation
- Thick stratum corneum that cracks, flakes

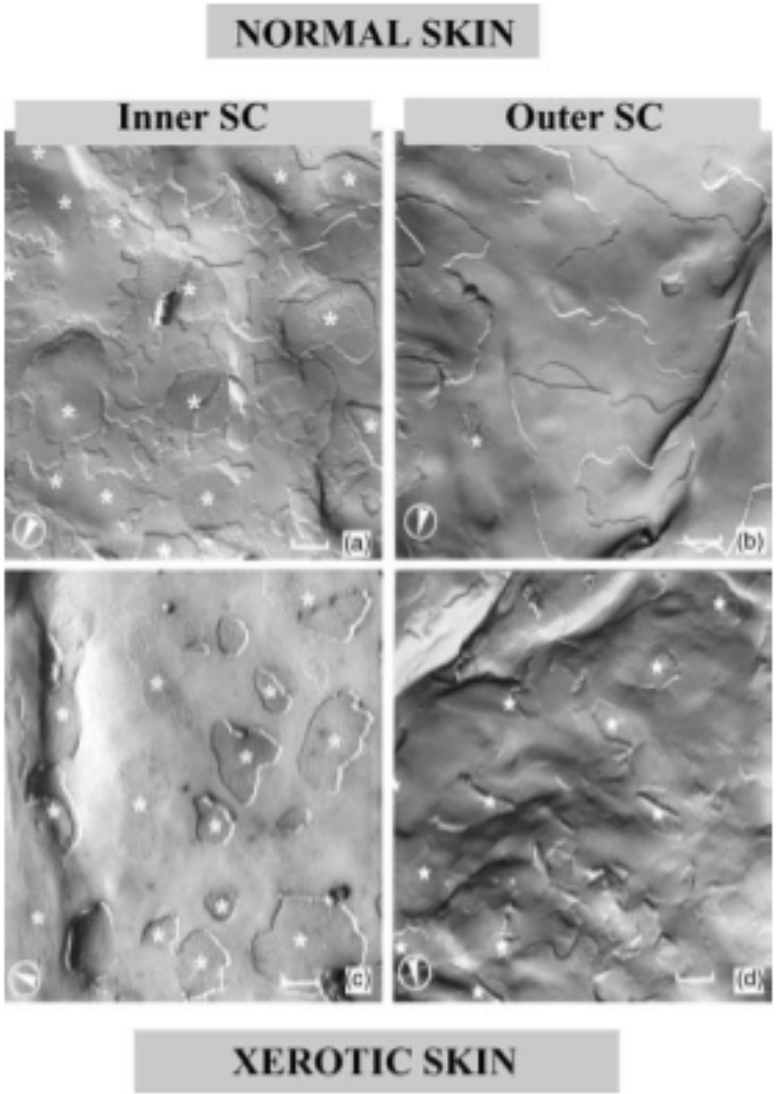
CHANGES IN S.C. IN DRY SKIN

- Impaired degradation of corneodesmosomes
  - Increased number of corneodesmosomes
  - Irregular appearance of corneodesmosomes
- Decrease of ceramide levels
  - Influence of lamellar lipids on desquamatory enzymes
- Reduction of SCCE enzymes
  - Not true for SLS induced dry skin
- Increased superficial pH
  - Reduced activity of desquamatory enzymes

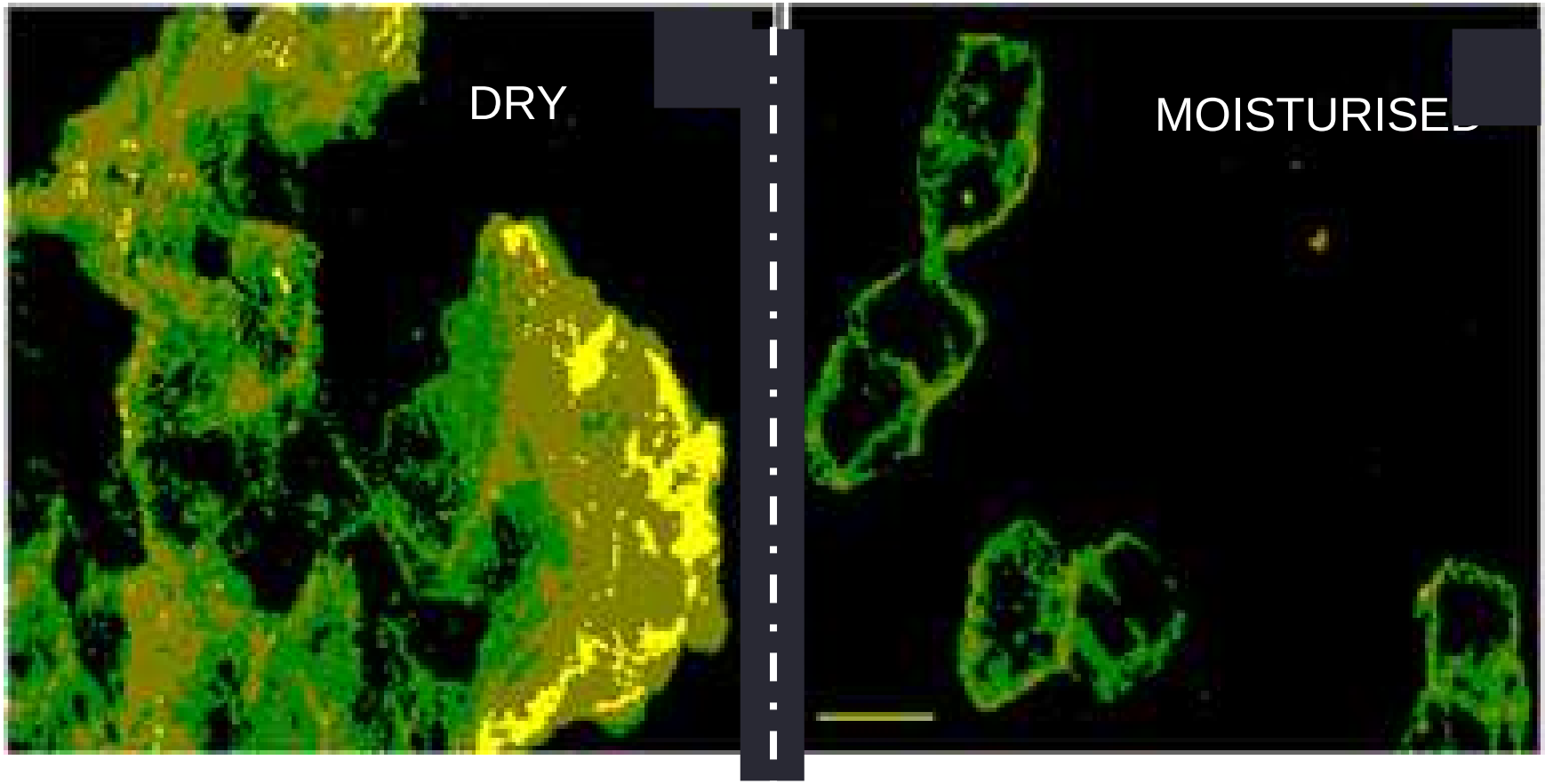
CORNEODESMOSOMES -EM



CORNEODESMOSOMES IN DRY SKIN



CORNEODESMOSOMAL HYDROLYSIS IS PERTURBED IN DRY SKIN

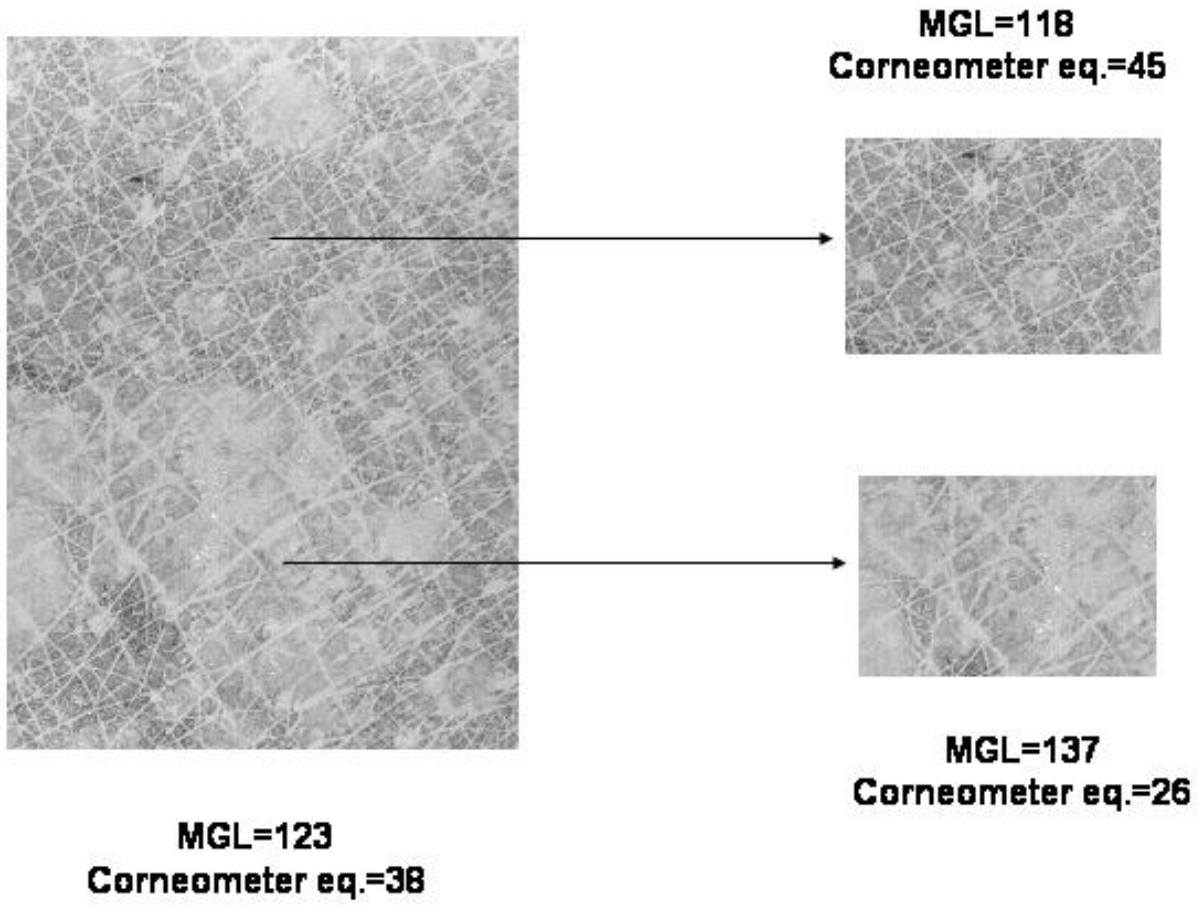


Intact corneocytes recovered from soap-dried and moisturized SC from the same individual and stained with an anti-desmocolin-1 antibody (component of corneodesmosomes)

DRY SKIN IN AGING

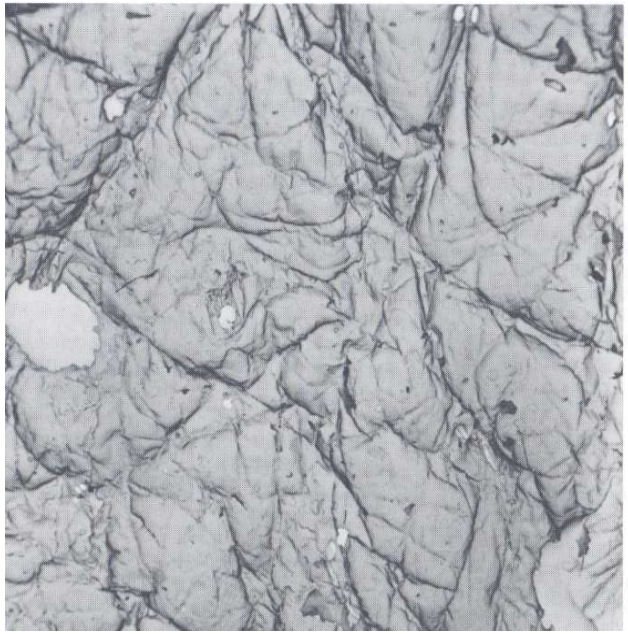
- Changes in corneocytes
- Alterations in intercellular lipids
- Alterations in keratinization and decrease of s.c. layers
- Decrease of water-binding factors (NMF etc..)

UNEVEN HYDRATION IN AGED SKIN



Batisse D et al., Skin Res Technol 2006

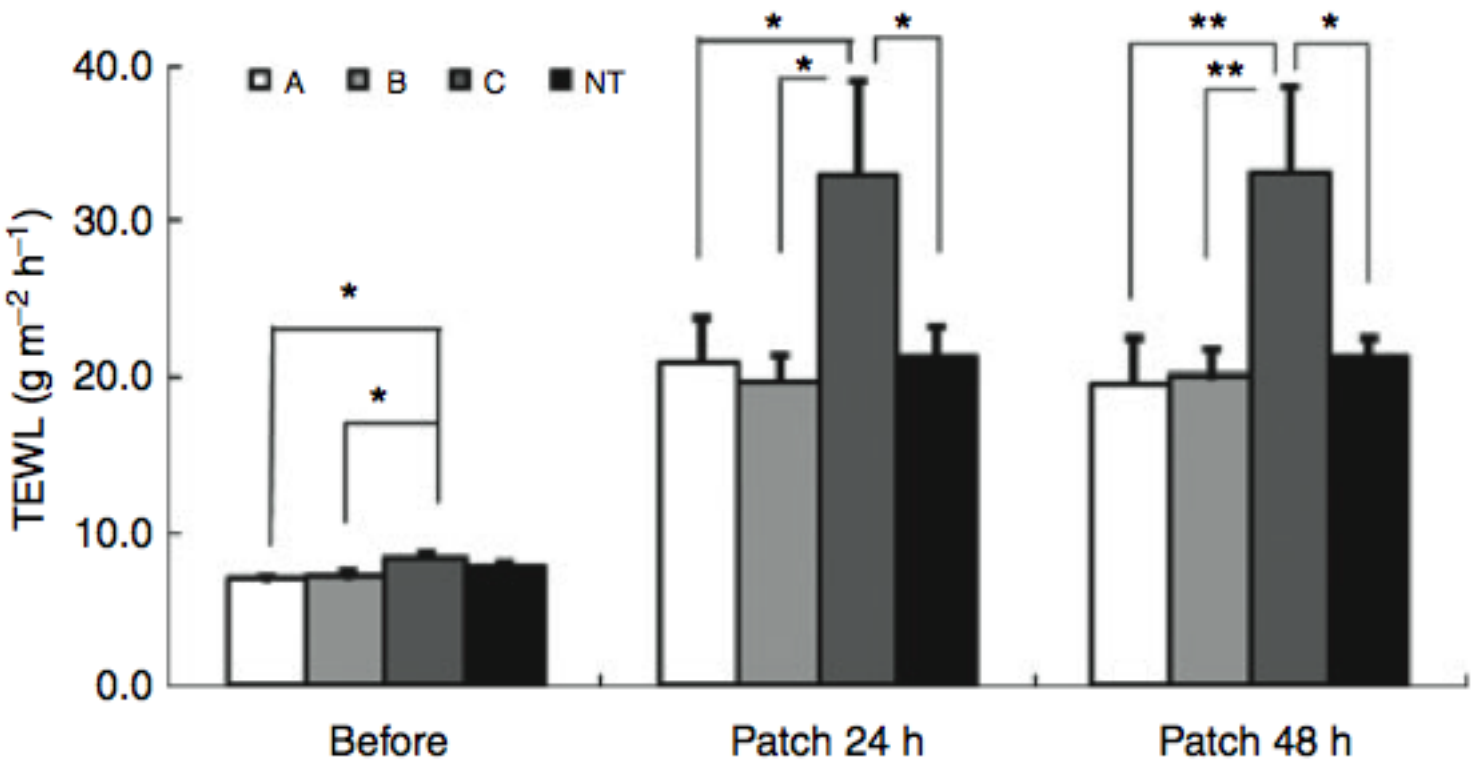
AFTER MOISTURIZING THERAPY



Basal

After 7 days

SLS-IRRITATION AFTER COSMETIC APPLICATION



Kim E et al, Int J Cosm Sci, 2009

PHYSIOLOGY OF WATER IN THE S.C.

- A properly hydrated state of SC improves the skin appearance (Agache and Humbert, 2004; Bernstein, 1996; Tagami, 2008).

- The SC water content plays a crucial role in maintaining many of the skin's biophysical properties (elasticity, distensibility) (Bouwstra et al., 2003; Harding, 2004; Pittet and Beau, 2002; Williams et al., 2007)

- Adequate skin hydration, in particular the superficial layer of the epidermis participates to the maintenance (maintains) the smoothness and softness of skin surface (Marty, 2002; Mazereeuw and Bonafe, 2002; Tagami, 2008).

PHYSIOLOGY OF WATER IN THE S.C.

- Absence of moisturization can have variable impact on an individual, including afterwash tightness sensation, lack of flexibility / extensibility, visible dryness (skin ashing), skin roughness, scaling, cracking, and ultimately, irritation in the form of visible erythema and itching (Ananthapadmanabhan et al., 2004; Bernstein, 1996; Williams et al., 2007).

- Decrease in stratum corneum water content causes improper desquamation and the appearance of dry, flaky skin (Verdier-Sevrain and Bonte, 2007).

CONCLUSIONS

- Water content decreases from the deeper to the most superficial layer
- Stratum corneum presents lowest water content of the skin
- The SC is a key layer of the epidermis. It provides a mechanic, hydric, antioxidative, and anti-microbial barrier function (Le Bitoux and Haftek, 2008)
- The SC provides the major skin barrier to water loss and permeation of environmental substances
- Normal skin hydration modulates desquamation (a part of the renewal process) a key process in skin physiology