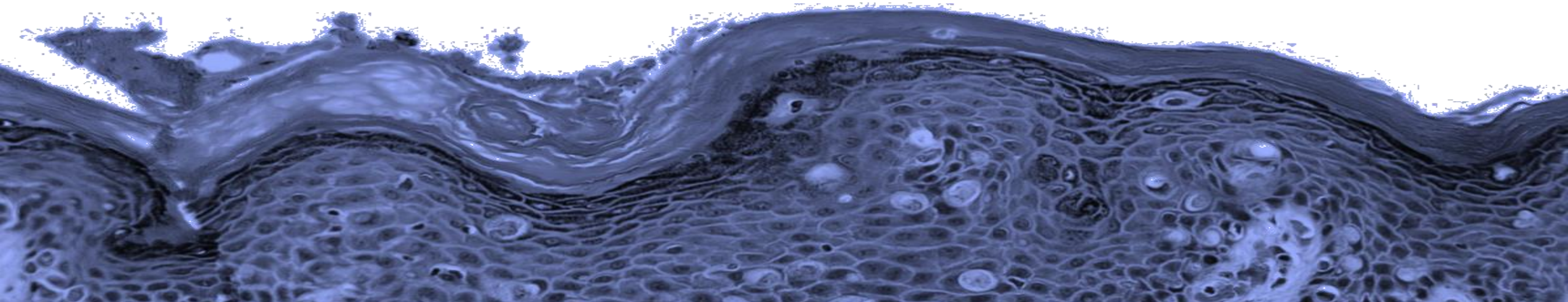
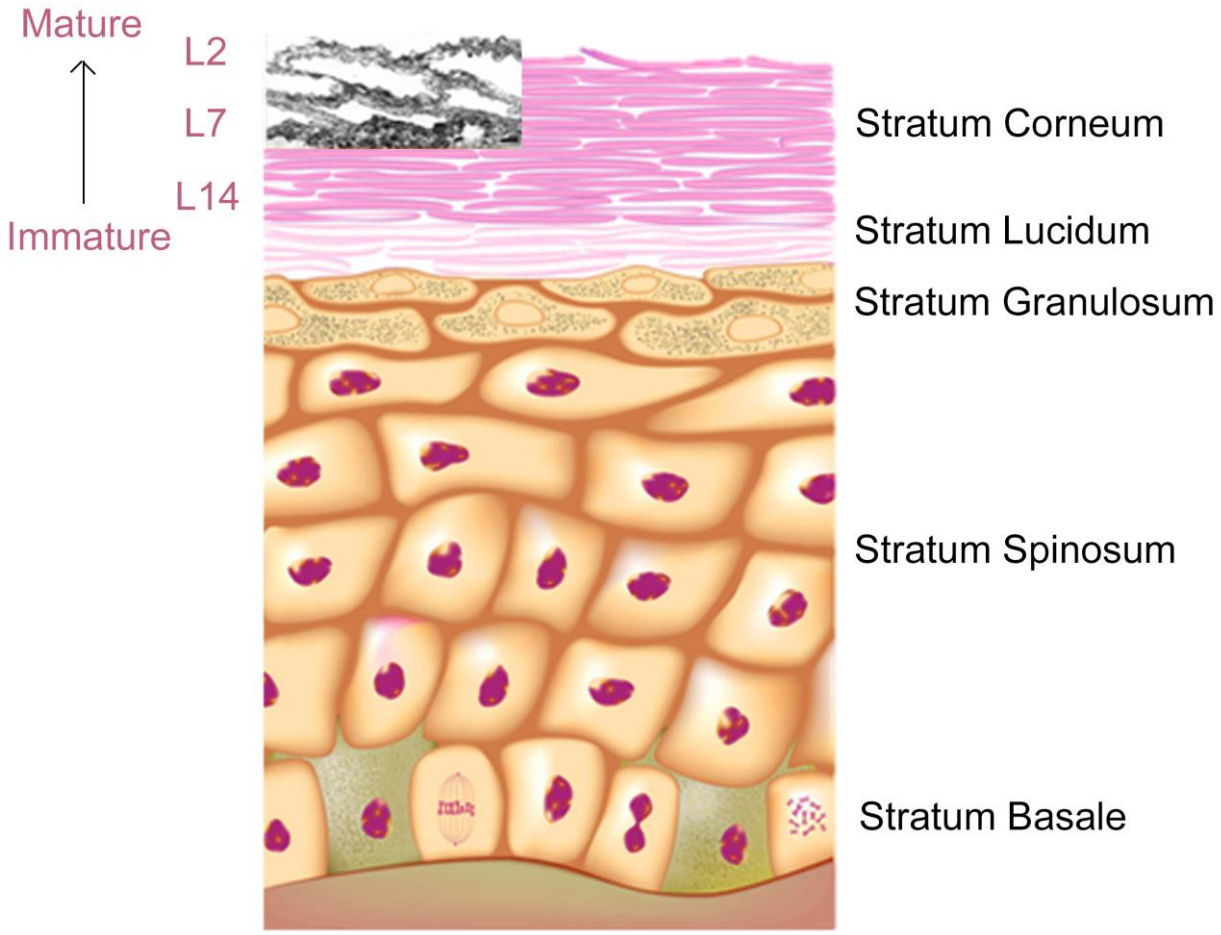
CORNEOCYTES NANO-MECHANICAL PROPERTIES CHANGES INDICATE ALTERATION OF THE SKIN BARRIER

Pascale MILANI, Anna Drillat, Julien CHLASTA, Rawad ABDAYEM,
Sanja KEZIC, and Marek HAFTEK

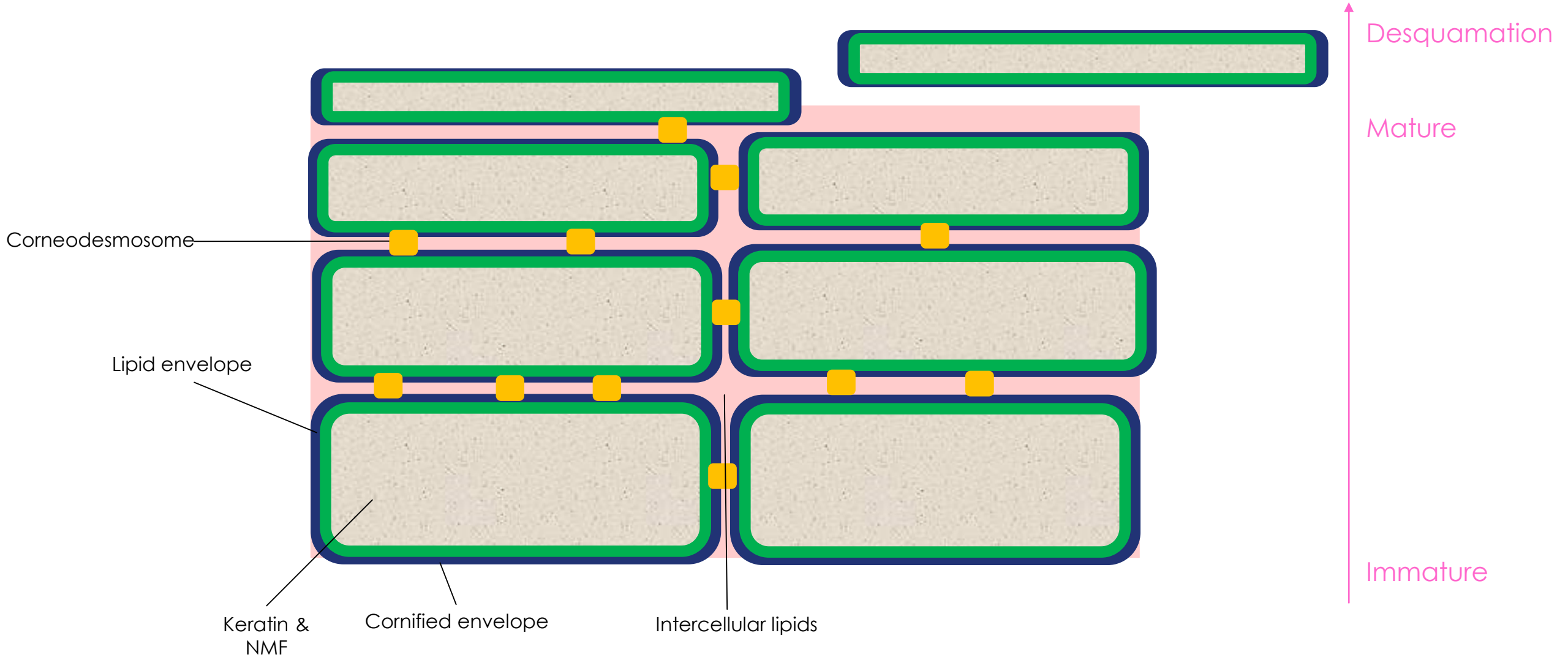


Stratum corneum: an essential physical barrier

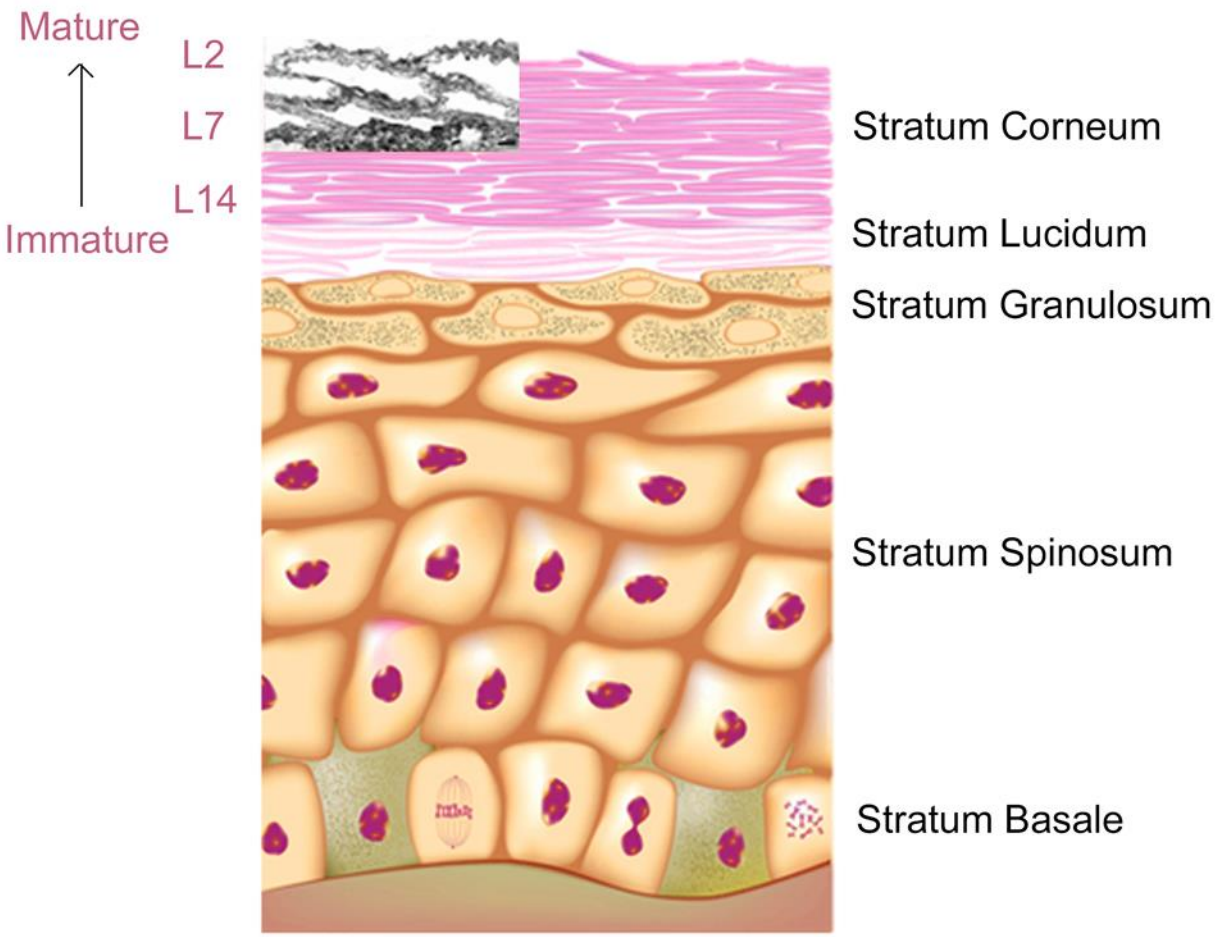


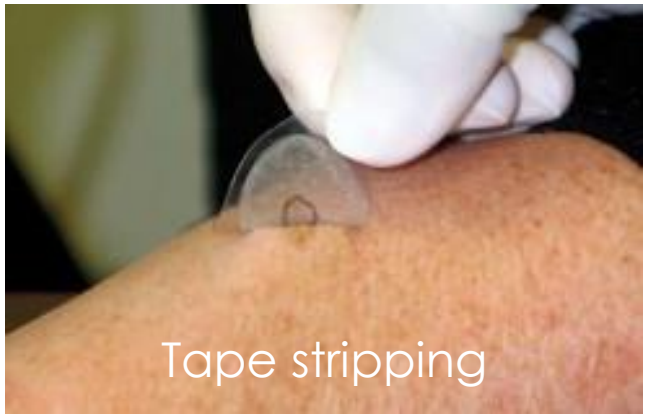
- Physical barrier – mechanical resistance
- Chemical barrier
- Water barrier
- Photoprotective barrier
- …

Stratum corneum: an essential physical barrier



Evaluation of barrier condition in a minimally invasive manner





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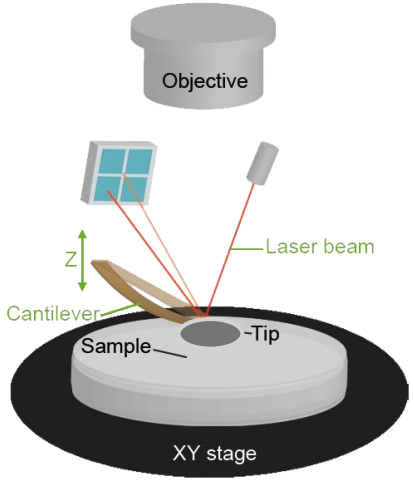
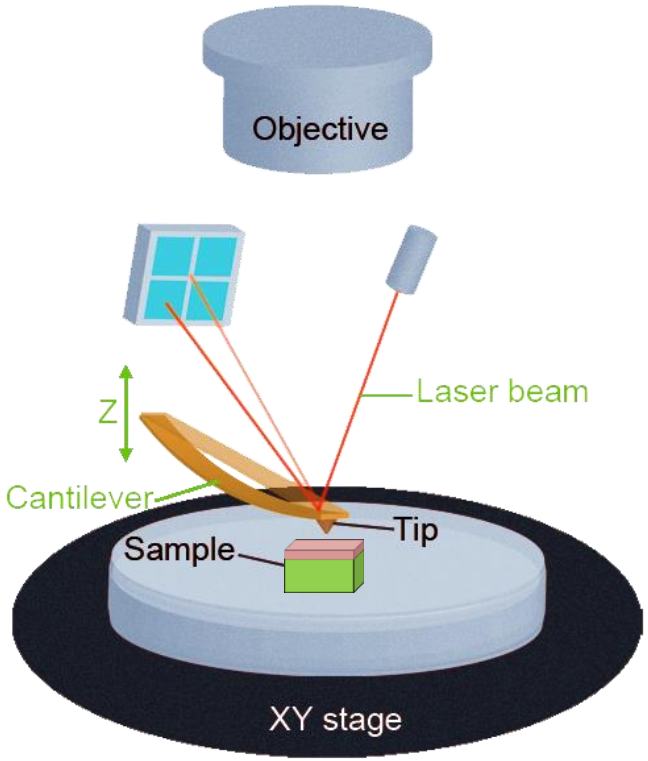
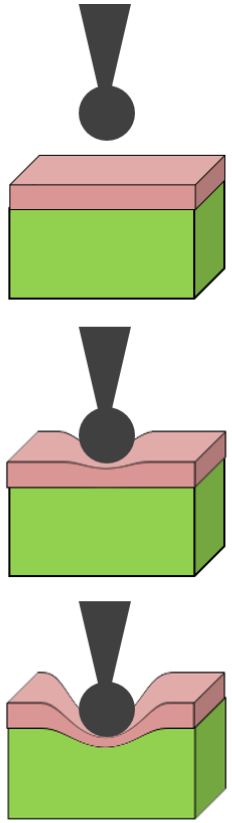
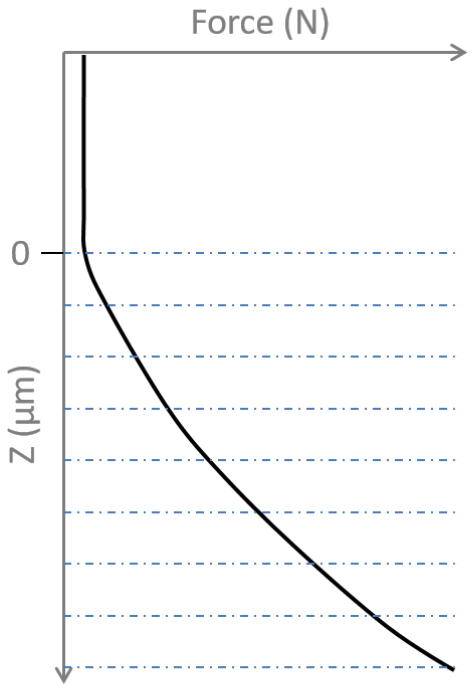
Atomic force microscopy

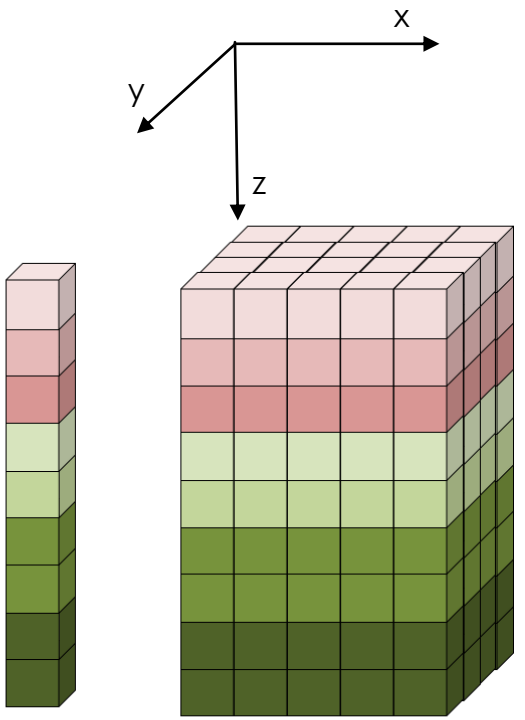


AFM operation









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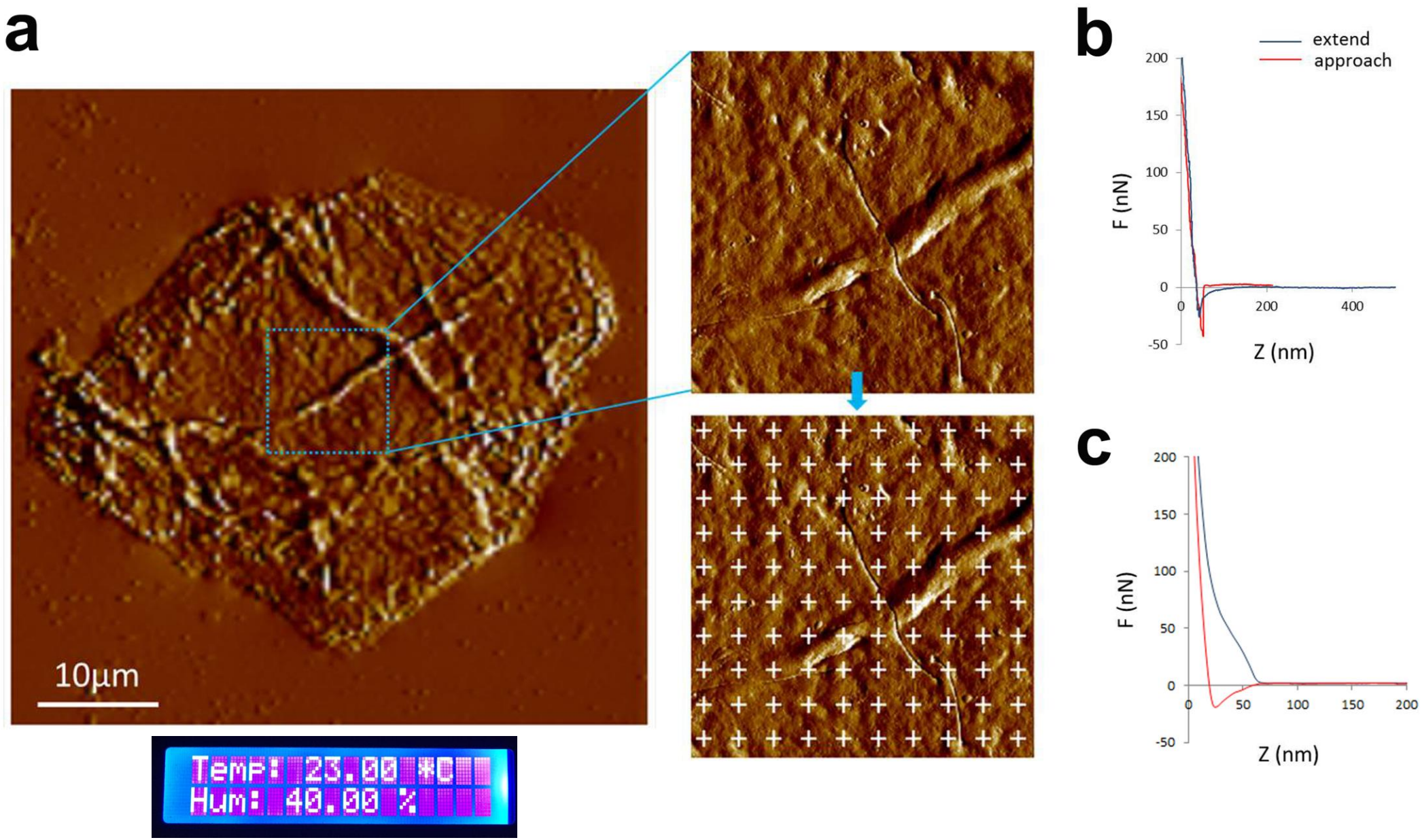
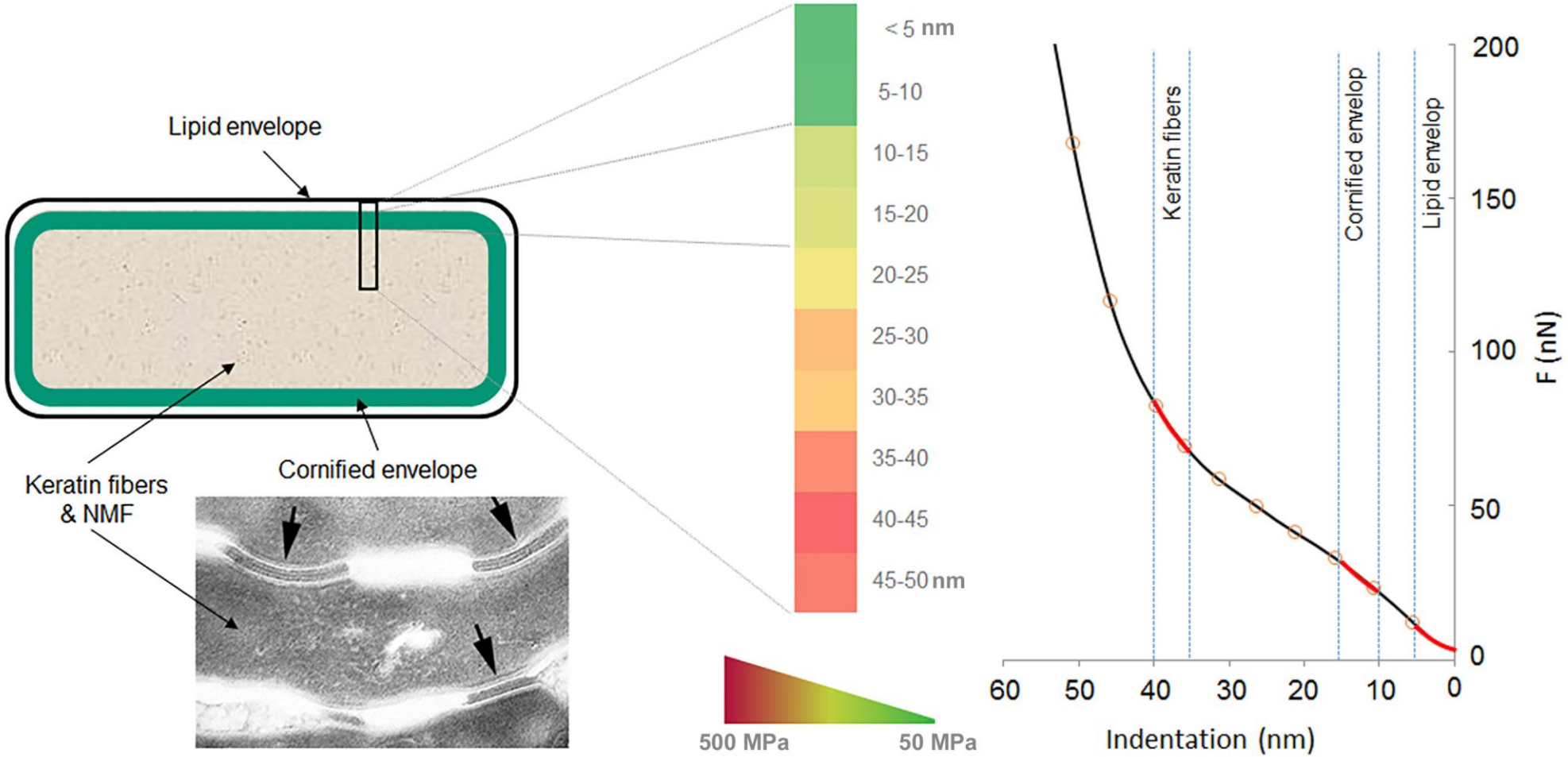
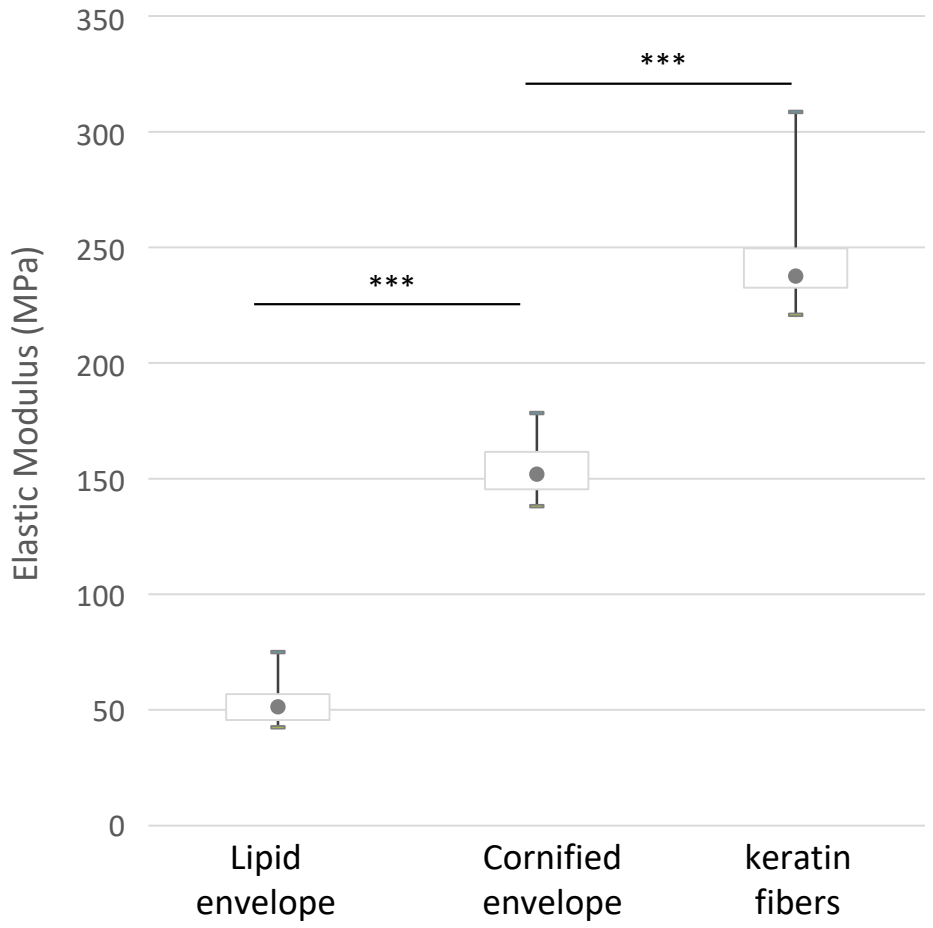


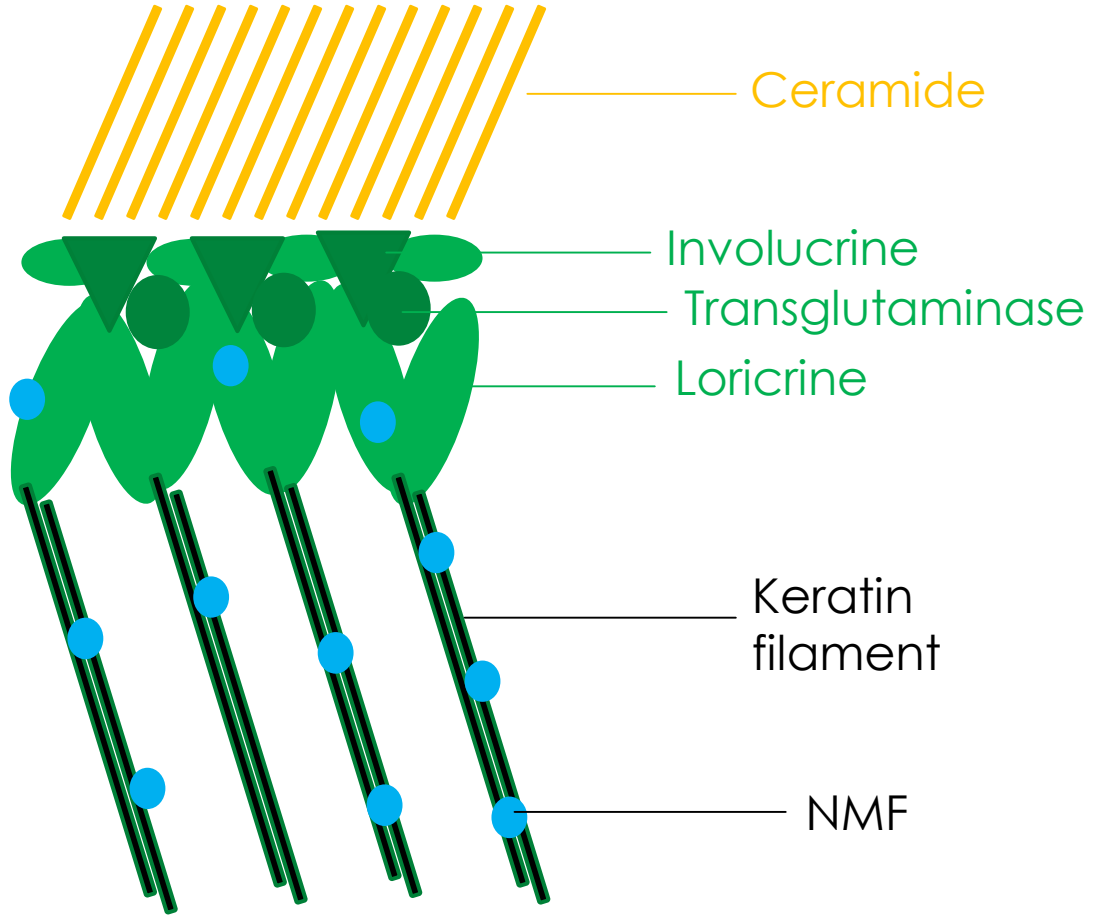
Evaluation of corneocytes mechanical properties



Milani et al, J. Mol. Rec. 2017

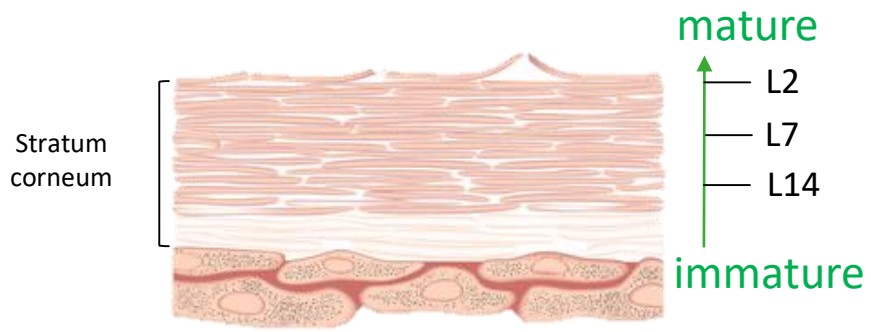
Evaluation of corneocytes mechanical properties



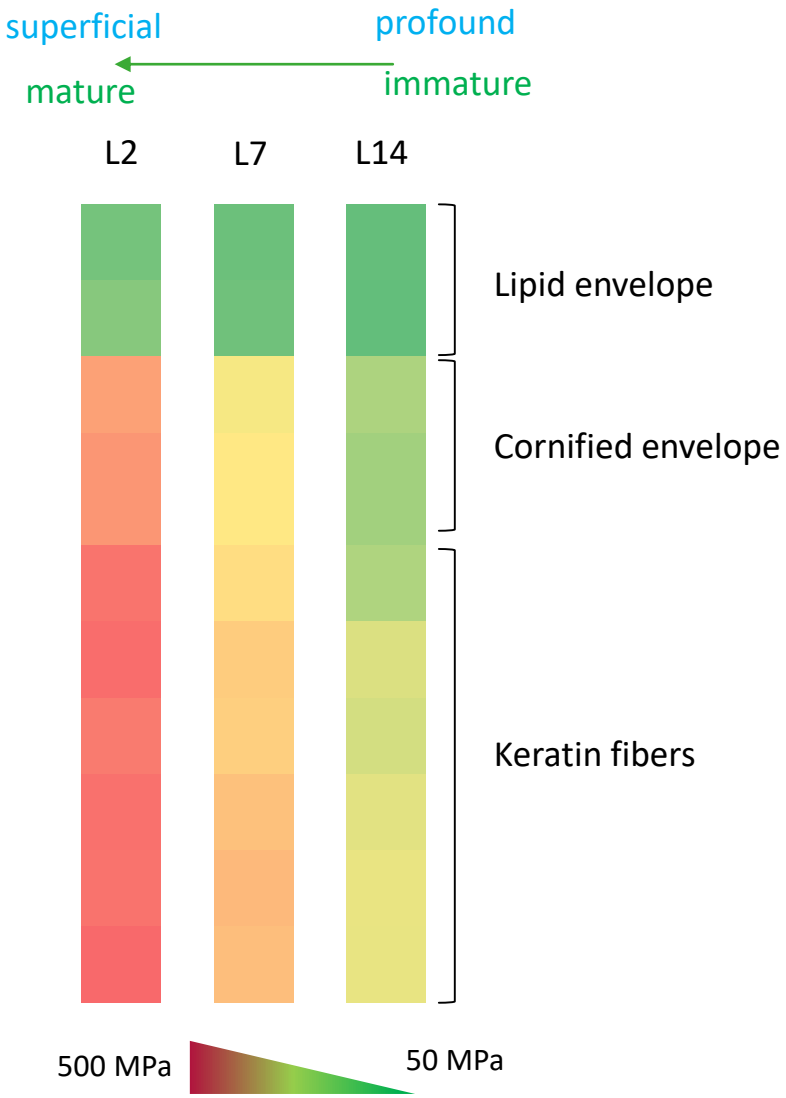


Milani et al, J. Mol. Rec. 2017

Exploration of the maturation process



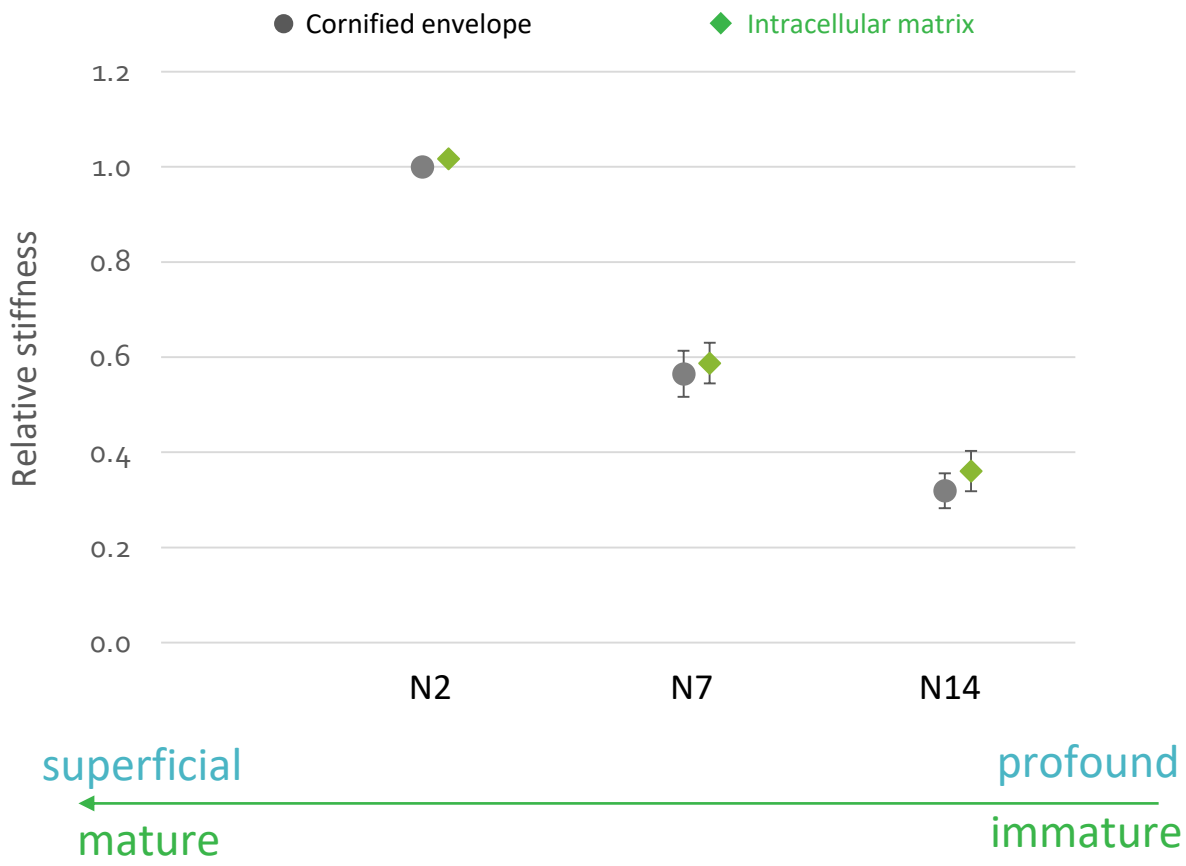
EXISTENCE OF DEPTH AND MATURATION-RELATED MECHANICAL CHANGES WITHIN THE SC



Milani et al, J. Mol. Rec. 2017

Exploration of the maturation process

THE RELATIVE STIFFNESS : AN INDICATION OF CORNEOCYTE MATURITY



Intracellular stiffness

CE stiffness

Milani et al, J. Mol. Rec. 2017

Exploration of the maturation process

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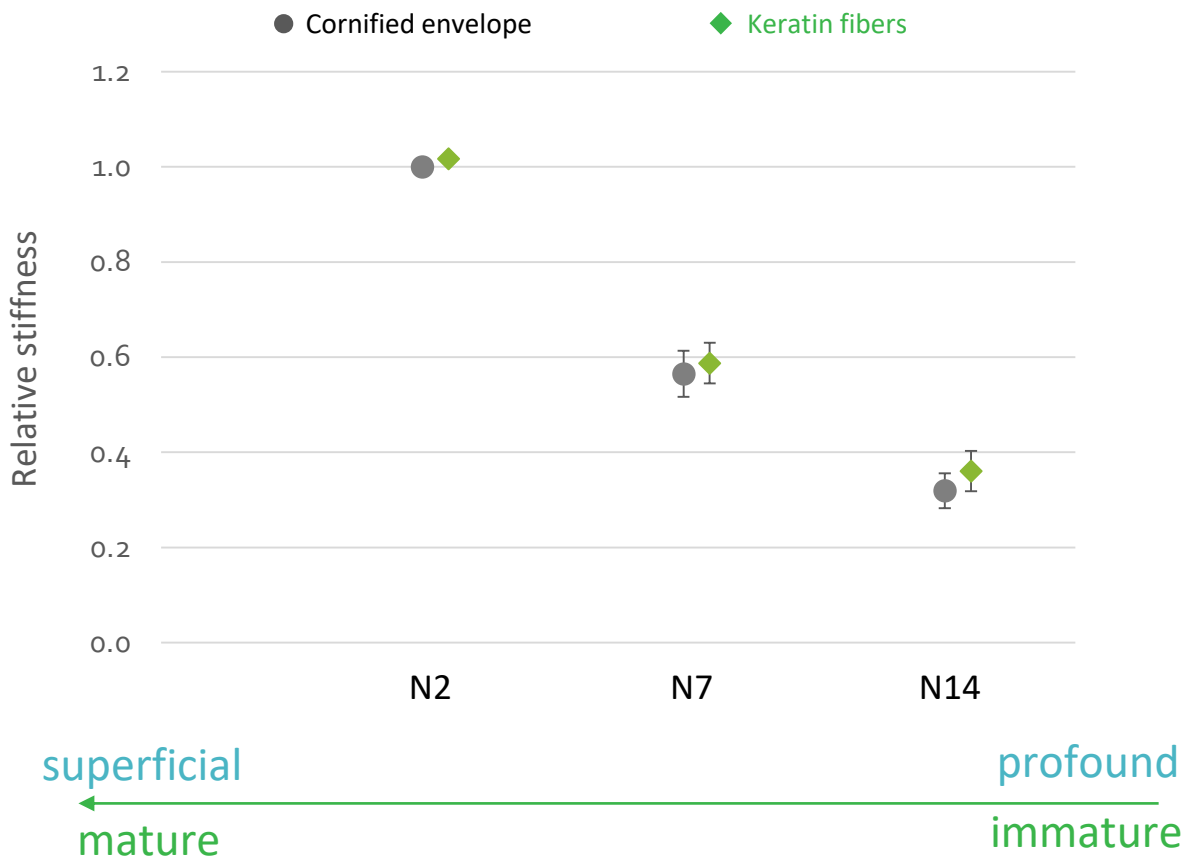

Intracellular stiffness

1. **Moisture gradient**

Milani et al, J. Mol. Rec. 2017

Exploration of the maturation process

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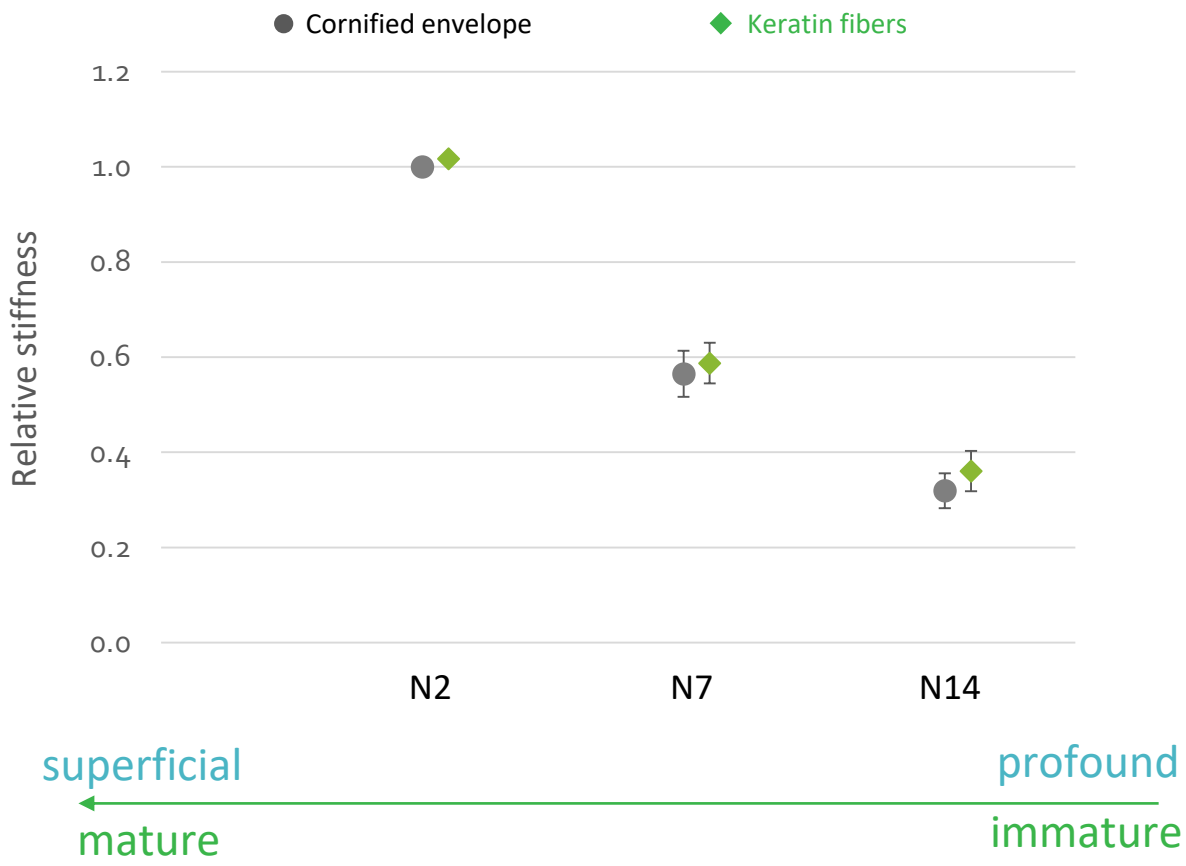

Intracellular stiffness

1. ~~Moisture gradient~~

Milani et al, J. Mol. Rec. 2017

Exploration of the maturation process

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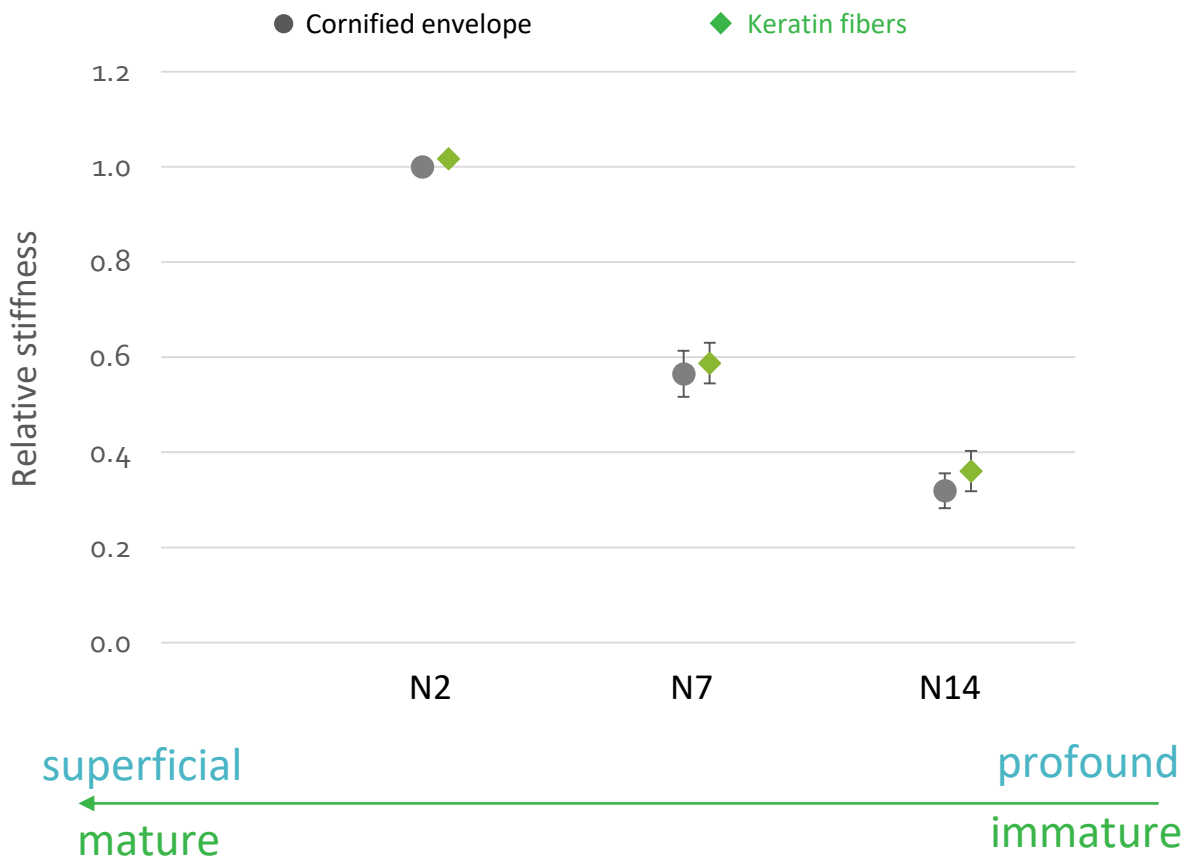


Intracellular stiffness

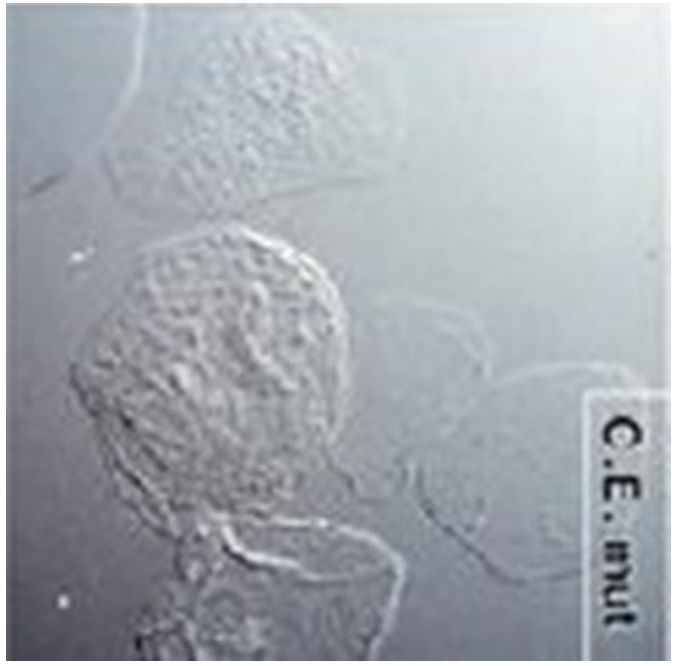
1. ~~**Moisture gradient**~~
2. **Water holding capacity**

- ❖ Ongoing enzymatic processing of filaggrin
- ❖ Folding and cross-linking of keratin filaments

Milani et al, J. Mol. Rec. 2017

Exploration of the maturation process

THE RELATIVE STIFFNESS : AN INDICATION OF CORNEOCYTE MATURITY

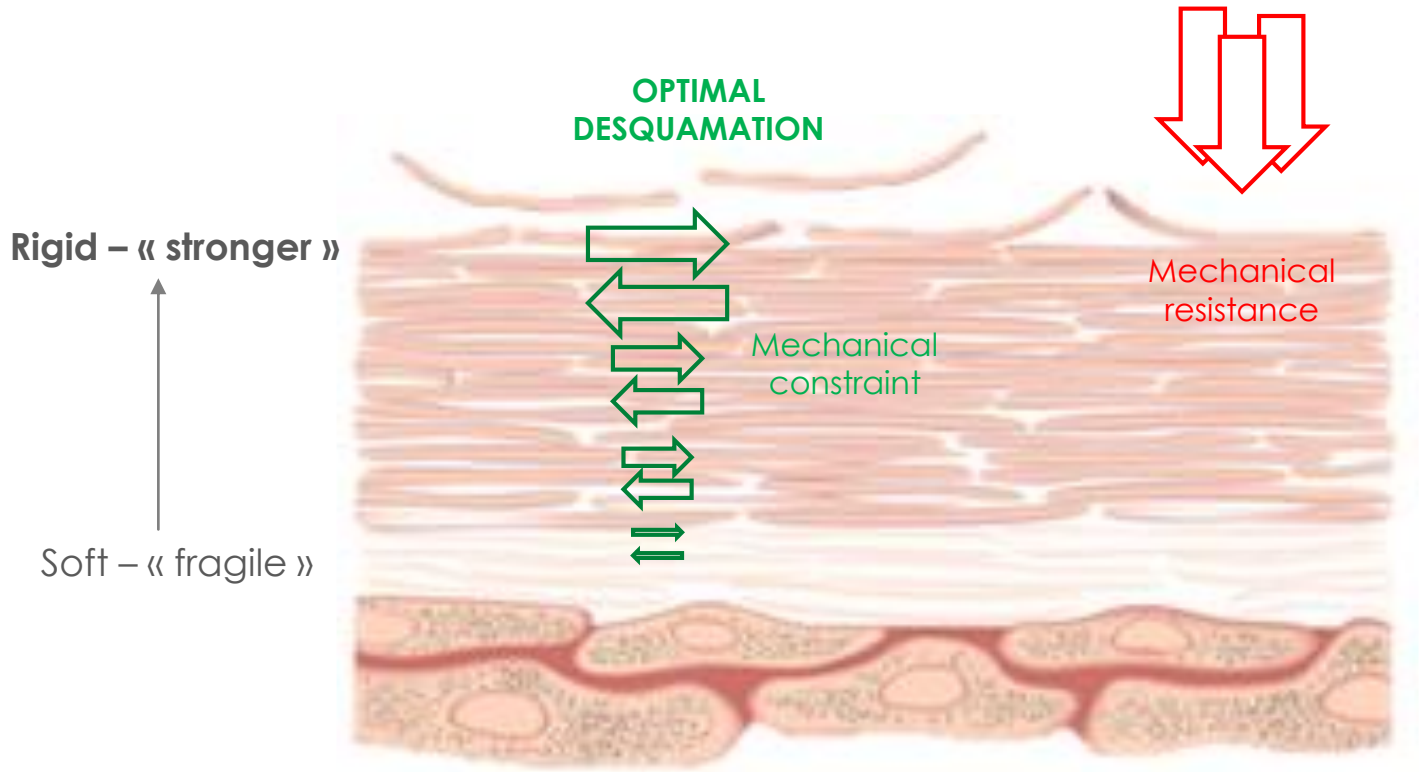


JA Segre et al, Nat Genet, 1999

1. **Cross-linking during maturation**

↗ **CE stiffness**

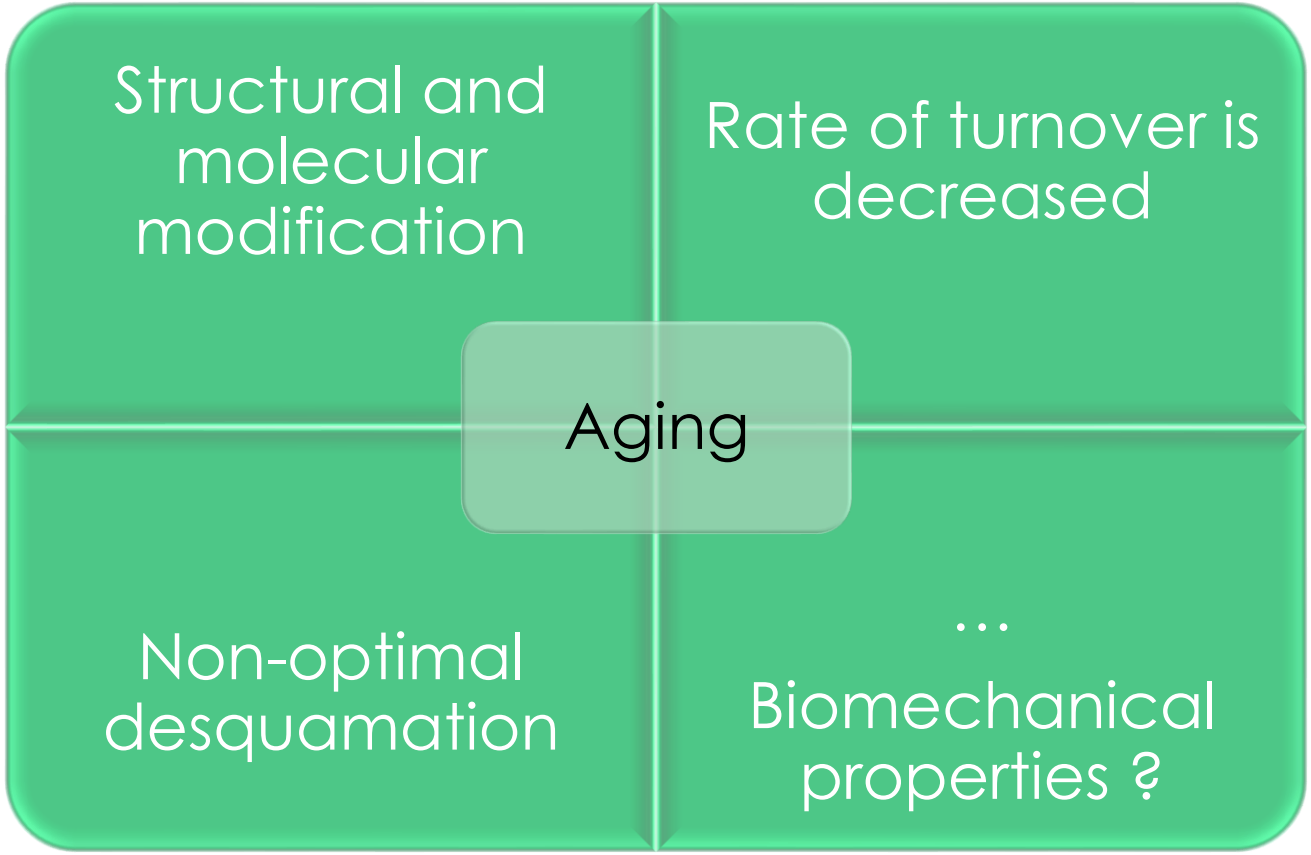
Exploration of the maturation process



1. **Physical-Mechanical barrier**

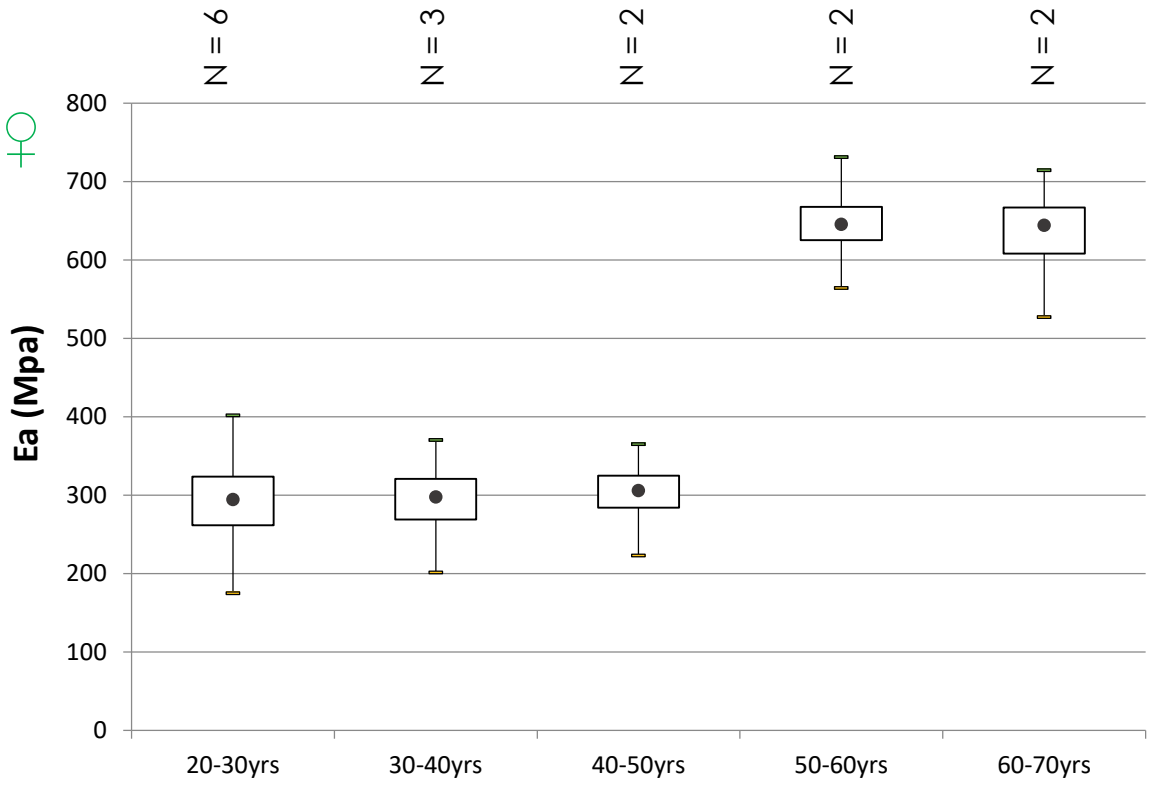
2. **Mechanical constraint likely contributes to proneness to desquamation**

Understanding age-induced mechanical alterations of the barrier

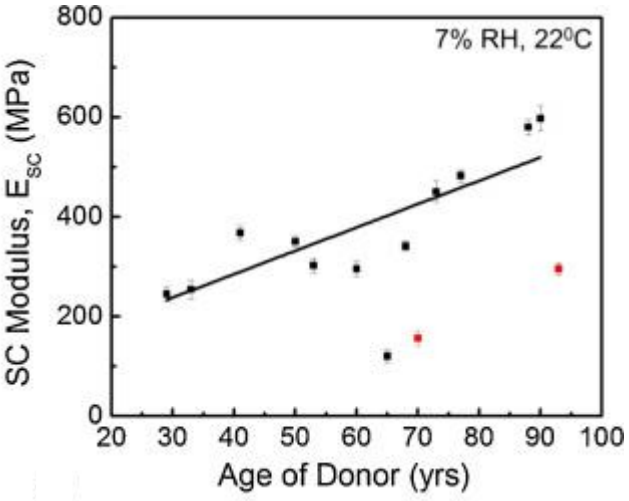


Understanding age-induced mechanical alterations of the barrier

Subcellular scale measurement



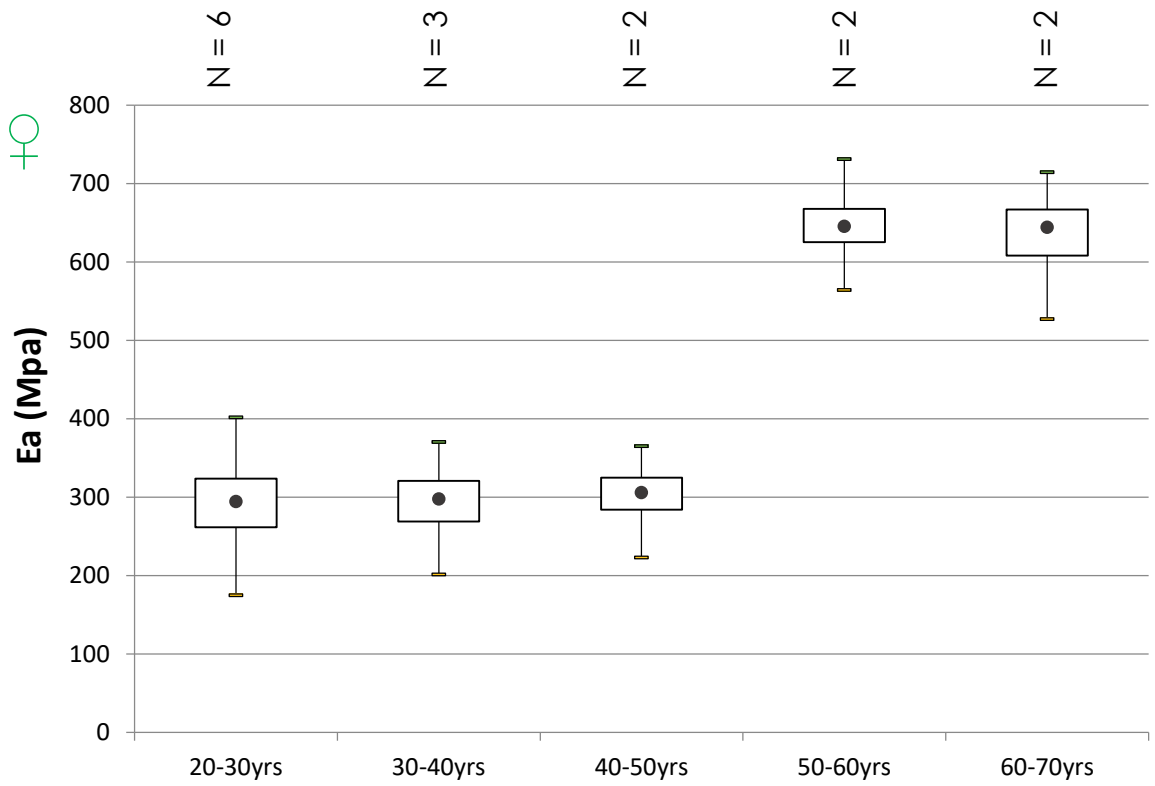
Overall mesure of the SC



Biniek et al. J of derm. 2015

CORNEOCYTE STIFFNESS INCREASES WITH AGE

Understanding age-induced mechanical alterations of the barrier



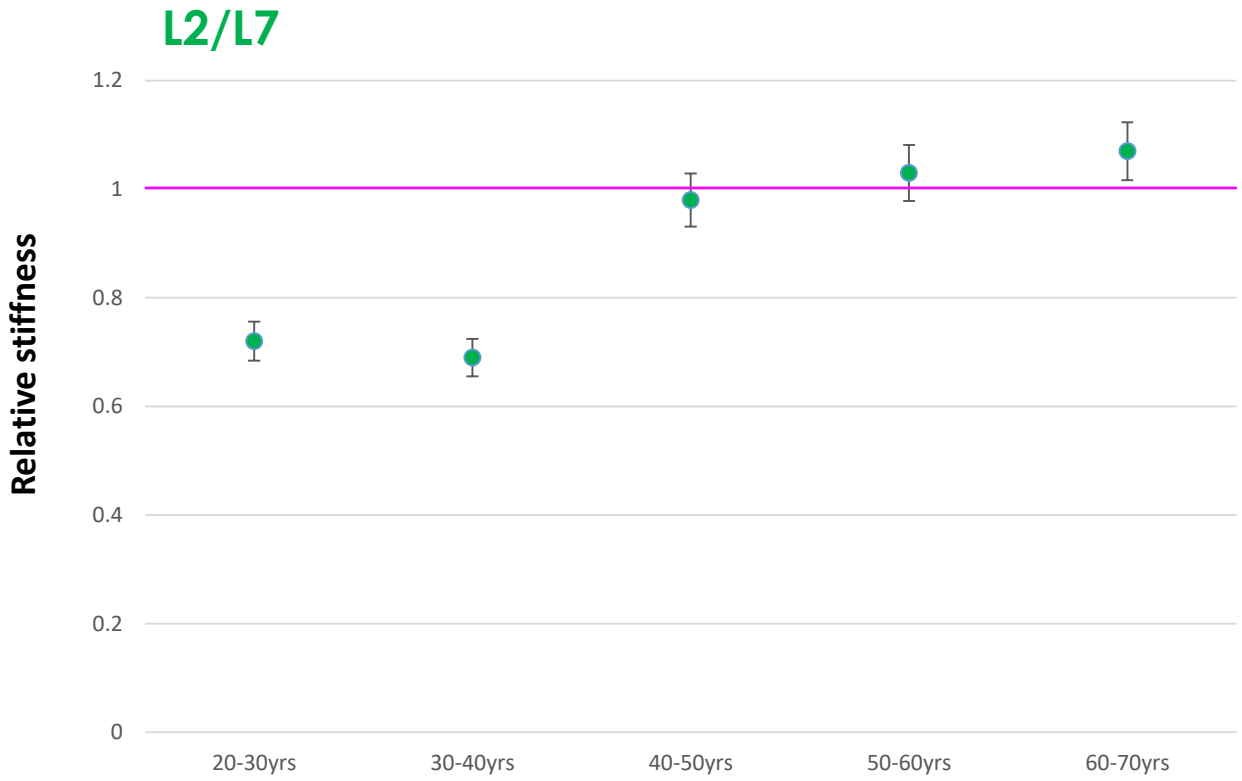
- **Cross-linking of keratin filaments**
  - Oxydation
  - Glycation
- **Decreasing water holding capacity**
  - Less NMFs
  - Increased intermolecular forces

CORNEOCYTE STIFFNESS INCREASES WITH AGE

Understanding age-induced mechanical alterations of the barrier

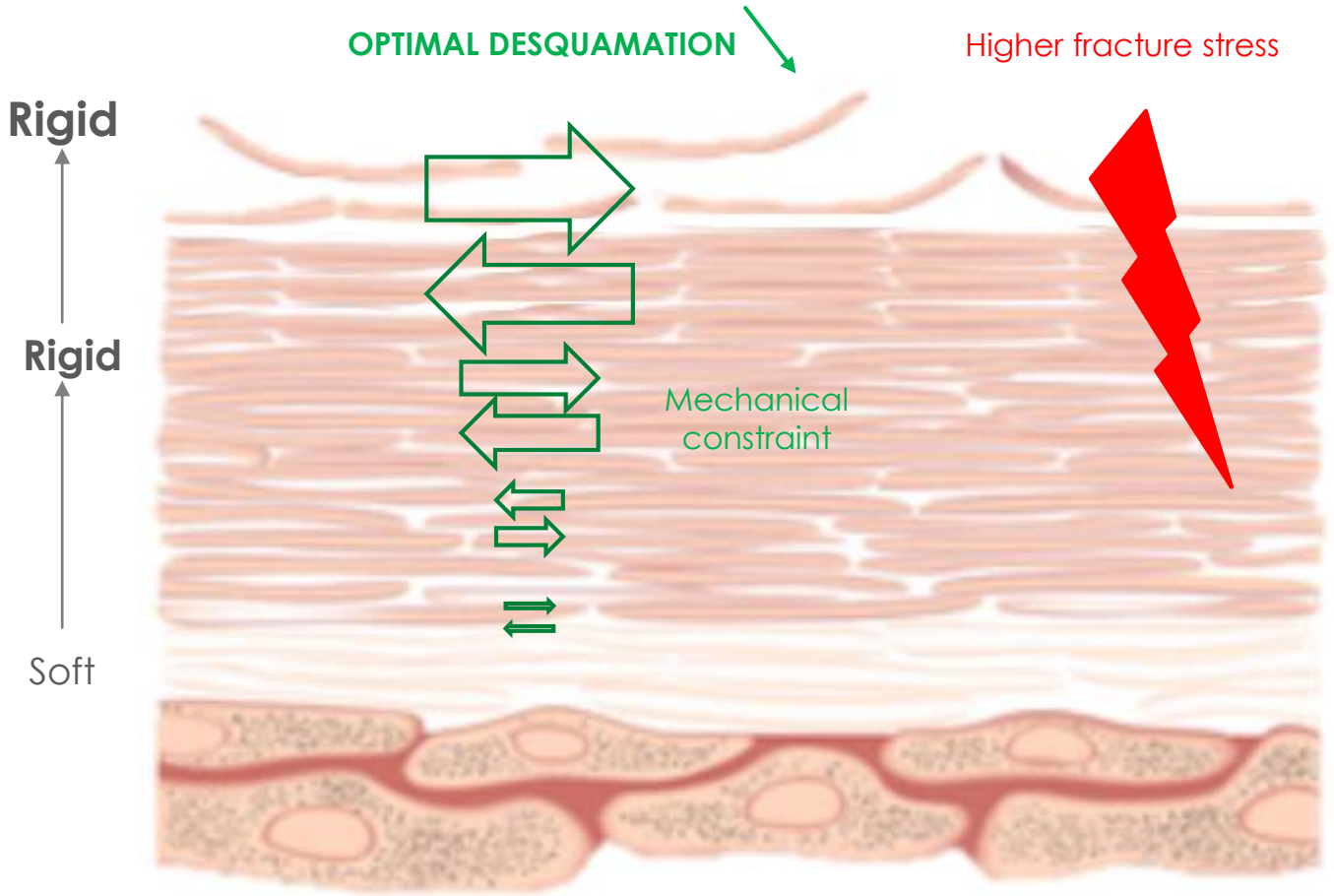
- ❑ **Less turnover**
- ❑ **Non-optimal desquamation**

❖ Accumulation of mature corneocytes



INTERNAL STIFFNESS GRADIENT IS DISRUPTED

Understanding age-induced mechanical alterations of the barrier



SC undergoes significant alterations

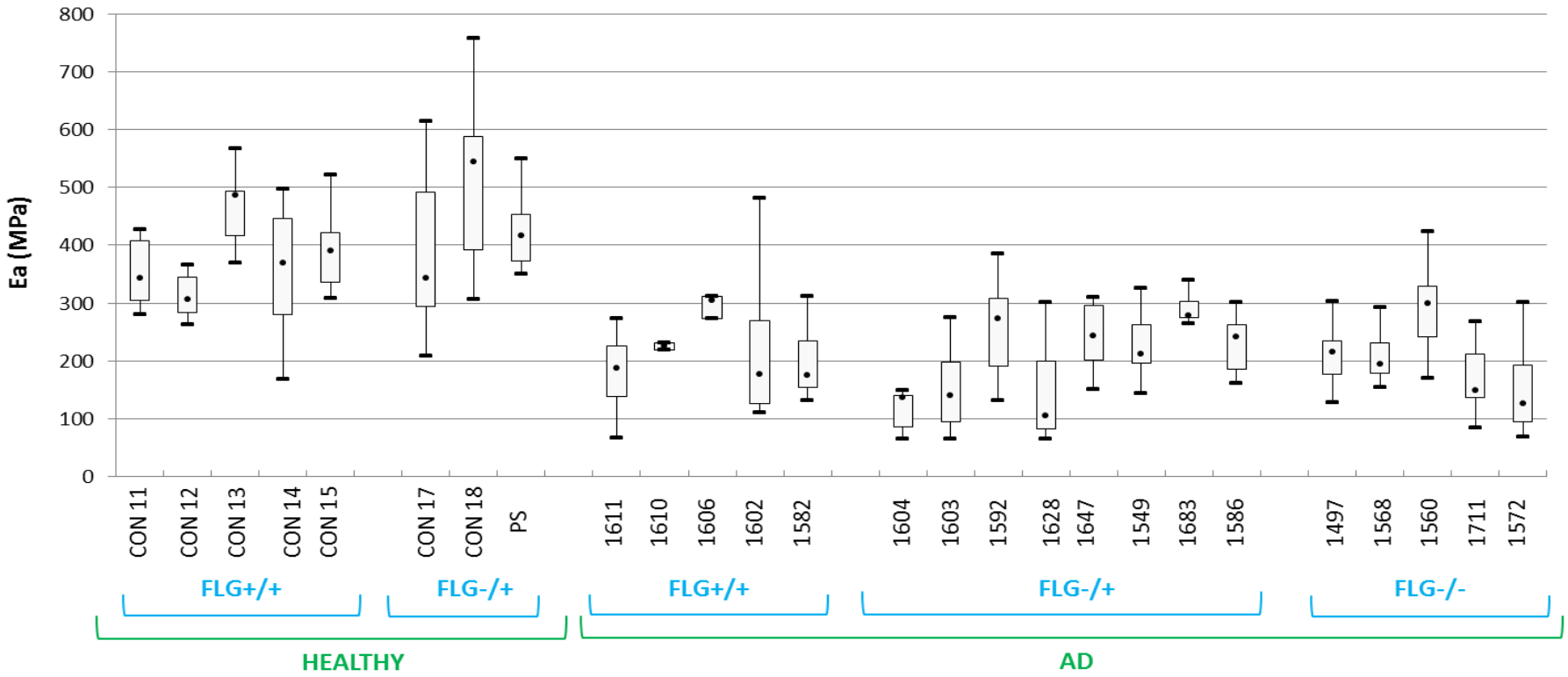
1. **Stiffer with higher frature stress**
2. **Non-optimal desquamation**

Characterization of barrier dysfunction: atopic dermatitis

- ❑ Disrupted epidermal terminal differentiation
- ❑ Deficiency of structurale proteins
- ❑ Reduced lipids
- ❑ Abnormal skin barrier
- ❑ Inflammation

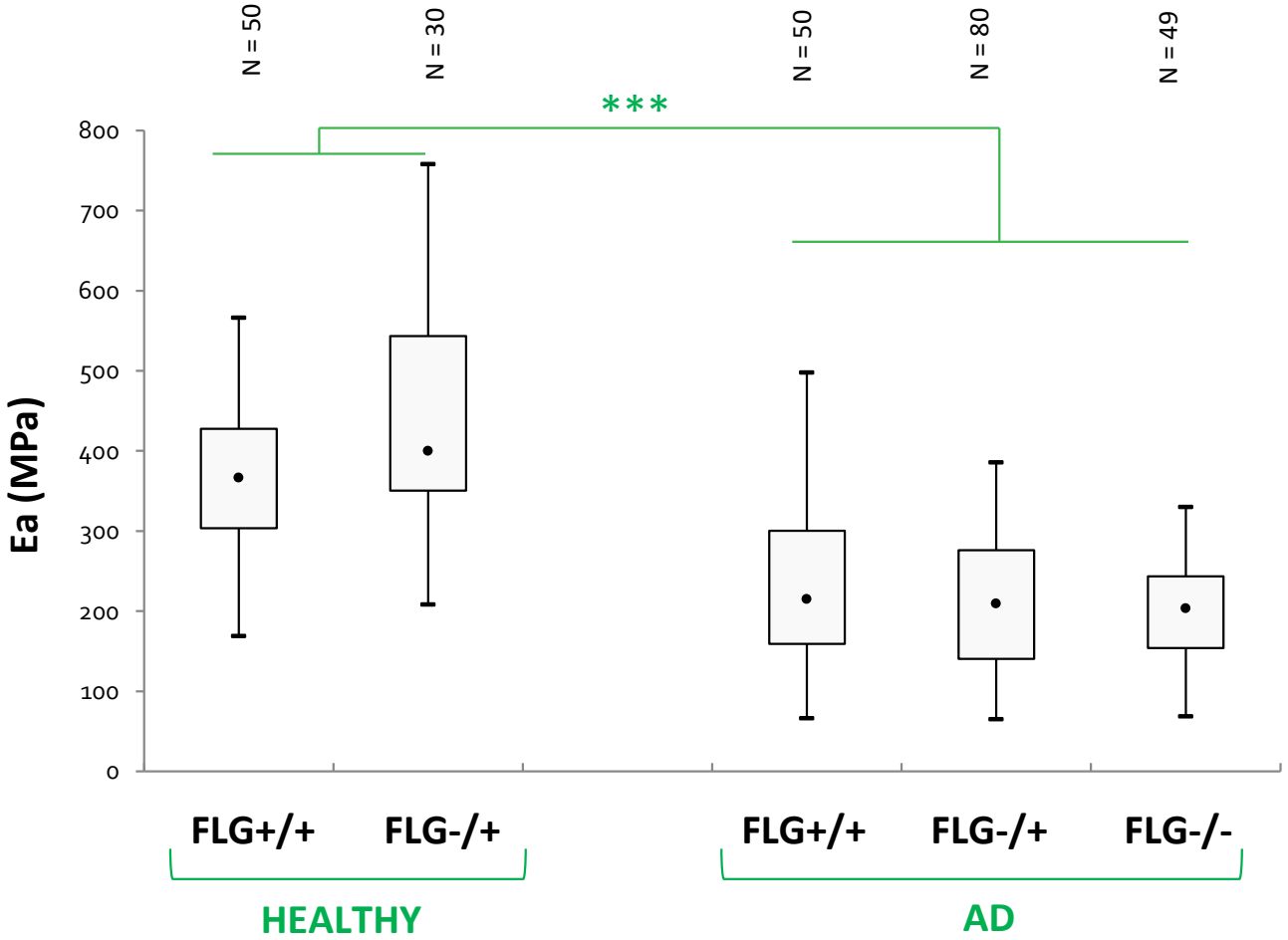
- ❖ GENETIC (FLG)
- ❖ ENVIRONNEMENT
- ❖ IMMUNOLOGIC FACTORS…

Characterization of barrier dysfunction: atopic dermatitis



Haftek et al, in preparation

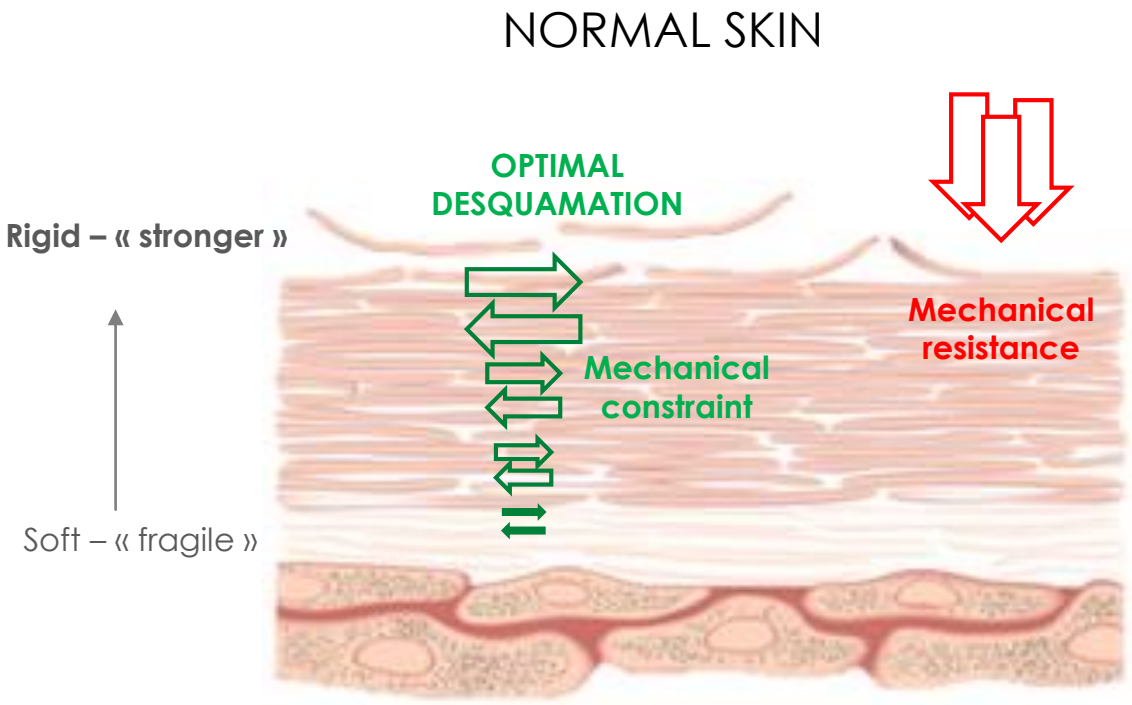
Characterization of barrier dysfunction: atopic dermatitis

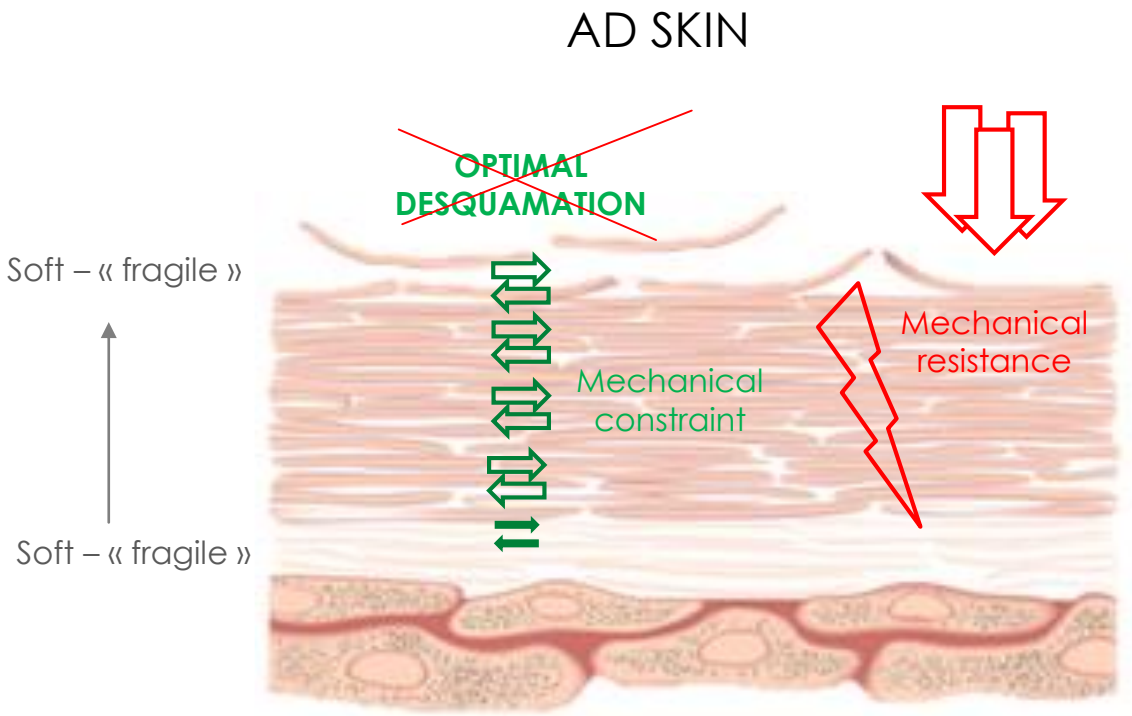


AD CORNEOCYTES ARE SOFTER

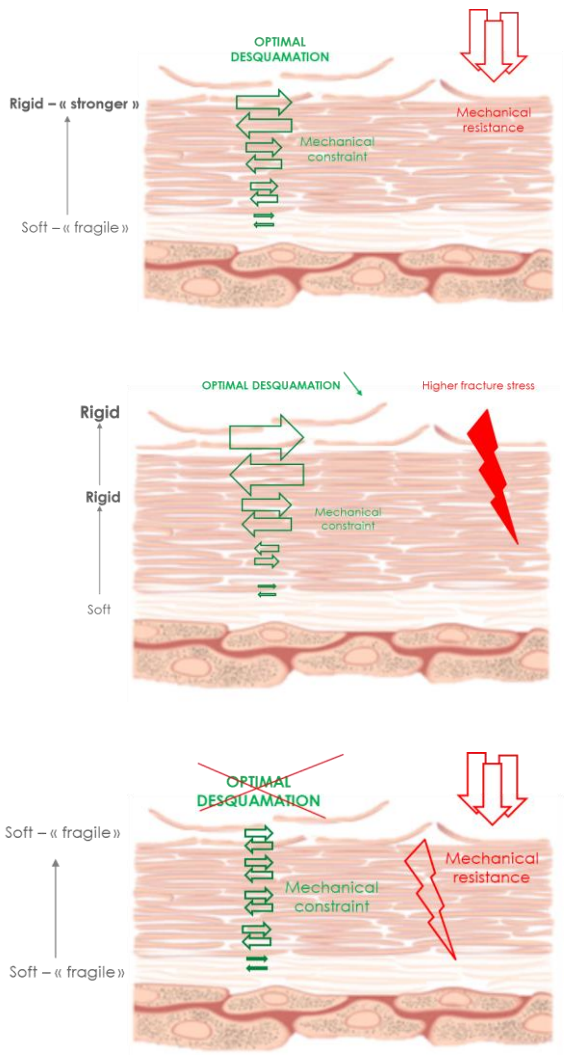
Haftek et al, in preparation

Characterization of barrier dysfunction: atopic dermatitis





Conclusions



- The relative stiffness of corneocytes appears to be linked to their maturity level
- The rigidity of superficial corneocytes may likely contribute to their proneness to optimal desquamation
- Age induced accumulation of stiff corneocytes at the surface
- Corneocytes from AD patients presented a lower stiffness than healthy subjects
- This approach can be used for minimally invasive evaluation of various skin conditions and exploring the mode of action of pharmacological or cosmetic ingredients.

Thanks you for attention

AD samples were collected in Dublin , Ireland,
in Prof. Alan Irvine's Dept .

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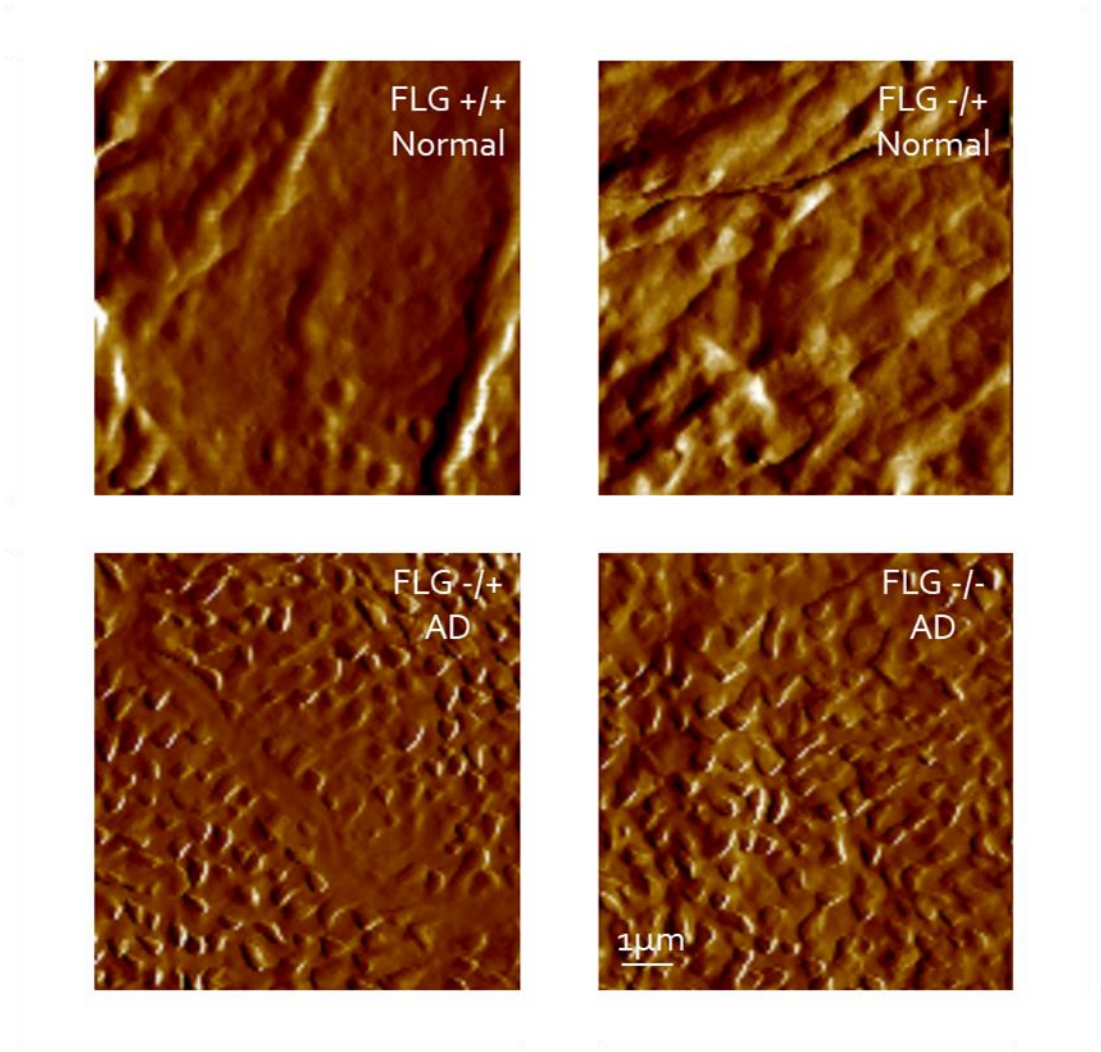
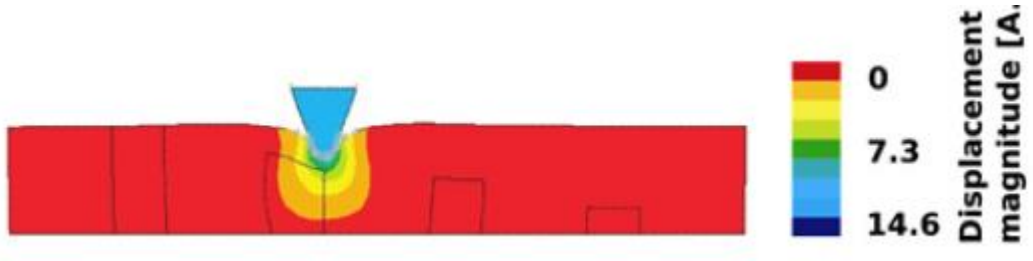
Characterization of barrier dysfunction: atopic dermatitis

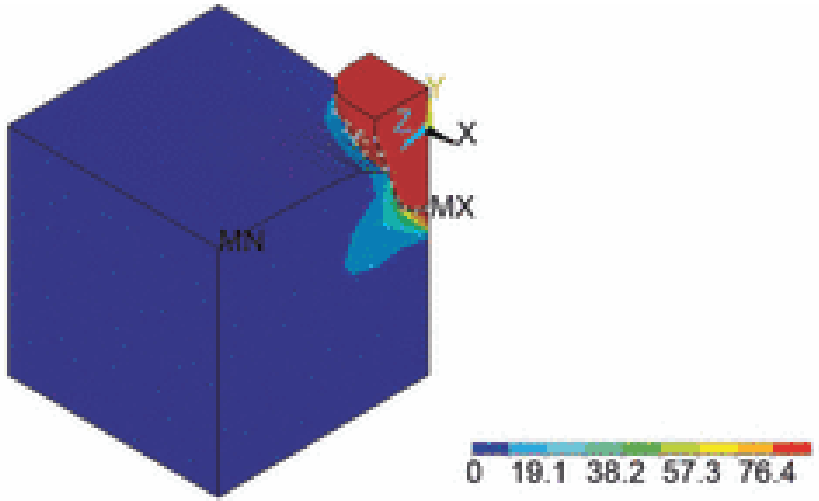


Supplemental data

SIMULATION BY FINITE ELEMENTS



Extracted from Roduit et al.,2009



Extracted from Milani et al.,2011

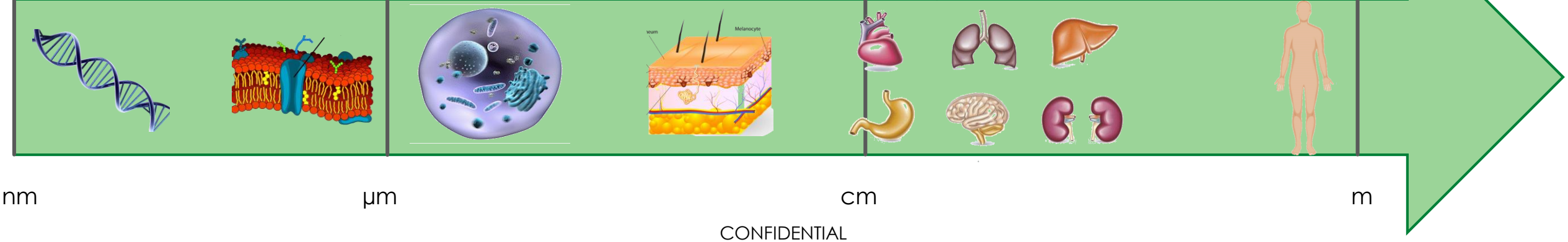
cutometer

AFM

Indenter

Micro indenter

Traction,Tension and Suction assay



nm µm cm m