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Phenotypic changes in the *corneome* and *ceramidome* of photo-damaged dry facial stratum corneum from different ethnic groups

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Introduction

Dry facial skin remains a major concern to consumers globally despite decades of moisturizer development. This is probably a result of two issues: most stratum corneum (SC) understanding in this respect is on body skin rather than facial skin and the biochemical changes in such conditions have largely been conducted on an analyte by analyte basis rather than global changes in analyte composition. The use of mass spectrometry-based 'omic' approaches is on the increase for investigating skin biochemistry, especially proteomics and lipidomics. However, these approaches have not been used to study both the corneome and ceramidome of facial SC. Our aim was to utilise methods to understand more precisely the effects of SC maturation (Figure 1) and its relation to facial photodamage, skin pigmentation and ethnicity and to explain some of these differences.

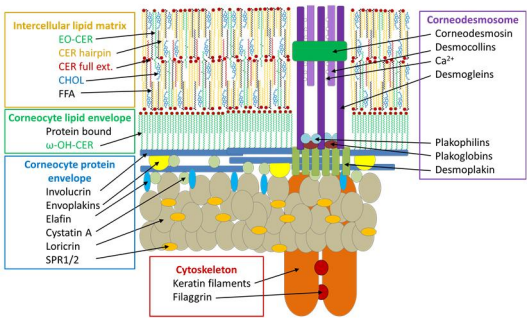

Figure 1: Key elements of SC cornification: the cytoskeleton, the corneocyte protein envelope (CPE), the corneocyte lipid envelope (CLE), the intercellular lipid matrix and the corneodesmosomes. The corneodesmosomes are degraded by proteases enabling desquamation, the final stage of SC maturation. By courtesy of Thomas Schmitt, University Halle, DE.

Materials and methods

Sixty healthy female volunteers, living in Pretoria, South Africa participated in this observation. There were three age- and count-matched groups of Albino African (40.3±2.9 years old), Black African (38.2±2.3 years old) and Caucasian subjects (44.6±3.1 years old) (Figure 2). Nine subsequent tape strippings were taken on the right cheek, 3 cm vertically beneath the outer edge of the eye. The first tape stripping each of 24 selected subjects (eight subjects per group) were analyzed by a mass-spectrometry based shotgun lipidomics platform to define the facial ceramidome and all nine tape strippings of eighteen selected subjects (six subjects per group) were pooled and analyzed by mass-spectrometry based proteomics to define the facial SC corneome.

Figure 2: Besides normally pigmented Caucasians (left) and Black Africans (center) we also enrolled Albino Africans (right) as an extreme model for pronounced photodamage in order to reveal the most relevant indications for the corresponding pathways and signaling molecules. Albino Africans had significantly increased facial TEWL and skin dryness, associated with reduced corneocyte maturation and size despite increased NMF levels.

Ceramidomics, results

Fatty acid / Sphingoid base	Non-hydroxy fatty acid [N]	α-hydroxy fatty acid [A]	Esterified ω-hydroxy fatty acid [EO]
Dihydrosphingosine [DS]	CER[NDS]	CER[ADS]	CER[EODS]
Sphingosine [S]	CER[NS]	CER[AS]	CER[EOS]
Phytosphingosine [P]	CER[NP]	CER[AP]	CER[EOP]
6-hydroxy sphingosine [H]	CER[NH]	CER[AH]	CER[EOH]

Figure 3: Structure of the major free ceramide classes of human SC. Each ceramide molecule is composed of a sphingoid base and a fatty acid residue.

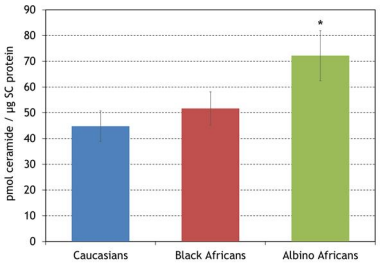

Figure 4: Total ceramide levels of Albino Africans were higher than those from normally pigmented Black Africans and Caucasians. Data are mean ± SEM, * p<0.05.

SC proteomics, results

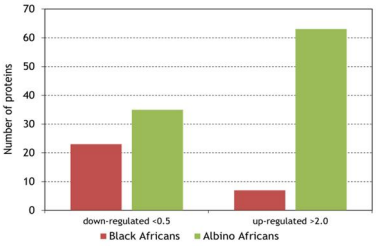

Figure 6: Number of proteins that were significantly (p<0.05) down-regulated <0.5 fold and up-regulated >2.0 fold compared to Caucasians. A total of 436 SC proteins were identified on the cheek in each of the three subject groups.

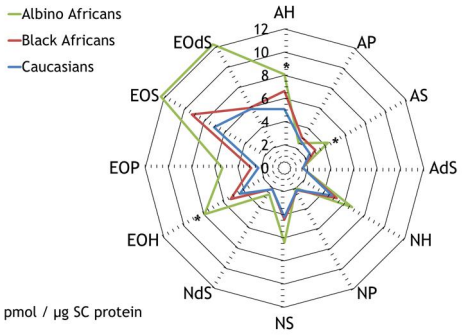

Figure 5: Comparison of the 12 different types of ceramides. CER AH, AS and EOH were significantly (p<0.05) elevated in Albino Africans with trends of increasing levels of CER NH, NS and EOP, EOS and EOdS.

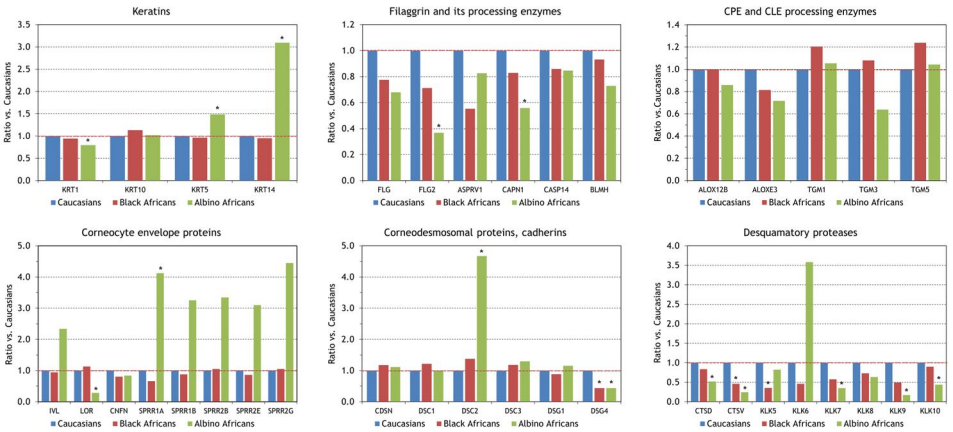

Figure 7: Comparison of protein quantities of protein families involved in SC differentiation and maturation. The proteins are listed as gene names and expressed as fold change vs. Caucasians, * p<0.05.

Discussion and conclusion

- There was a trend of reduced total ceramide levels in Caucasians compared to Black Africans.
- The total ceramide levels and particularly the long chain EO types were significantly increased in Albino Africans. The latter indicates a lack of their incorporation into the CPE, confirmed by the reduced levels of the CLE maturation enzymes ALOX12B and ALOXE3.
- Both African groups showed reduced levels of filaggrin proteins and their processing enzymes, explaining the better hydrated skin in Black but not at all in Albino Africans.
- Increased KRT5/14 and decreased KRT1 indicate keratinocyte hyperproliferation and reduced differentiation in Albino Africans.
- Reduced loricrin and increased SRRR levels indicate major changes to the CPE in Albino Africans.
- Lower levels of desquamatory proteases in both African groups and increased DSC2 levels in Albinos explain their increased SC thickness compared to Caucasians.
- Interestingly even CTSV was lower in the Black Africans compared with the Caucasians.

Reduced corneocyte maturation is a major problem of photodamaged facial skin.

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