INTRODUCTION

- Serine proteases drive stratum corneum (SC) desquamation through the proteolysis of corneodesmosomes.1 2
- Two key corneodesmosome adhesion proteins, desmoglein 1 and desmocollin 1, are degraded by trypsin-like and chymotrypsin-like serine proteases to facilitate corneocyte sloughing.2
- In the lower SC, the stratum compactum, corneodesmosomes cover the SC surface uniformly. As corneocytes mature and progress upwards through the SC, the corneodesmosomes become degraded. In the uppermost layers of the SC, the stratum disjunctum, only the peripheral corneodesmosomes remain.2
- SC pH is an important regulator of skin barrier homeostasis, and when elevated increases the activity of serine proteases, which in turn accelerates corneodesmosome proteolysis, resulting in barrier breakdown.3 4
- We aimed to investigate the consequences of elevated SC protease activity in atopic dermatitis (AD) and soap-induced xerosis at the SC surface.

METHODS

2 cohorts were recruited. Cohort 1, a non-atopic control group (n=12) and an active AD group (n=12). Cohort 2 was non-atopic and underwent an exaggerated washing regimen to induce xerosis on one forearm using an alkyl carboxylate soap, leaving the other forearm untreated (n=5).
- Desmoglein 1 and desmocollin 1 distribution was determined by immunofluorescence on samples of SC removed by tape stripping, and scored using Image J (see Figure 2).
- Desmoglein 1 and desmocollin 1 distribution was determined for samples of SC removed by tape stripping. Samples were stained with anti-DSC1 (Santa Cruz Biotechnology) and Alexa Fluor 488 (Life Technologies). Samples were observed using an inverted Zeiss LSM 510 NLO confocal microscope, and scored as uniform or more peripheral (see Figure 2).

RESULTS

Figure 3: Mean distribution of corneodesmosome adhesion proteins. Desmoglein 1 distribution was more uniform in AD and more peripheral in soap-induced xerosis (right). Significance was identified using non-parametric unpaired (AD) and paired (xerosis) t-tests.

Figure 4: Skin-surface pH was elevated in both AD and soap-induced xerosis.

Figure 5: Caseinolytic activity was elevated in AD but there was no significant change in soap-induced xerosis. Chymotrypsin-like activity was elevated in soap-induced xerosis but there was no significant change in AD. Finally, trypsin-like activity was elevated in AD. Significance was identified using non-parametric unpaired (AD) and paired (xerosis) t-tests.

Figure 6: Transepidermal water loss (TEWL), a measure of skin barrier function, was elevated in both AD and soap-induced xerosis, suggesting an impaired barrier in both conditions. Significance was identified using parametric unpaired (AD) and paired (xerosis) t-tests.

CONCLUSIONS

- In AD, broadly elevated protease activity leads to increased corneodesmosome degradation, resulting in a defective barrier with SC thinning and immature corneocytes exposed at the SC surface.
- In soap-induced xerosis, elevation of chymotrypsin-like protease activity (but not broad-spectrum/caseinolytic activity) leads to increased degradation of all but the peripheral corneodesmosomes, leaving loosely adhered corneocytes in the upper SC, resulting in a defective barrier exhibiting the flaky characteristics of xerotic skin.

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REFERENCES

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Figure 2: Desmoglein 1 and Desmocollin 1 distribution across corneocytes: scored on a scale of 1 (uniform) to 4 (peripheral).

Figure 3: Mean distribution of corneodesmosome adhesion proteins. Desmoglein 1 distribution was more uniform in AD and more peripheral in soap-induced xerosis (right). Significance was identified using non-parametric unpaired (AD) and paired (xerosis) t-tests.

Figure 4: Skin-surface pH in both AD and soap-induced xerosis.

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Figure 7: Corneocyte size at the SC surface (left) and estimated SC thickness (right) were reduced in AD, but there was no significant change in soap-induced xerosis. Significance was identified using parametric unpaired (AD) and paired (xerosis) t-tests.

Abnormal corneodesmosome distribution in atopic dermatitis and soap-induced xerosis

A. Wigley1, K. Brown1, H. Wan1, M. J. Cork1, S. G. Danby1,2

1. The Academic Unit of Dermatology Research, Department of Infection, Immunology & Cardiovascular Disease, The University of Sheffield, Sheffield, UK.
2. The Paediatric Dermatology Clinic, Sheffield Children’s Hospital, Sheffield, UK.

*Corresponding author: s.danby@sheffield.ac.uk