**Abnormal corneodesmosome distribution in atopic dermatitis and soap-induced xerosis**

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**Background:** In the stratum corneum (SC), inter-corneocyte cohesion is provided by corneodesmosomes. In healthy skin, corneodesmosomes are distributed uniformly across the corneocyte surface in the basal SC layers, becoming degraded as the corneocyte matures, leaving only peripheral corneodesmosomes at the SC surface. This gradual loss of corneocyte cohesion is regulated by numerous SC proteases to facilitate desquamation. In atopic dermatitis and soap-induced xerosis, there is abnormal corneodesmosome degradation.

**Objective:** To investigate the functional consequences of elevated proteases in the skin.

**Methods:** 2 cohorts were recruited. Cohort 1 contained a control group (n=12) and an AD group (n=12). Cohort 2 (n=5) induced xerosis using an alkyl carboxylate soap on one forearm, whilst leaving the other forearm untreated. Tape-strips collected from volar forearms were fluorescently stained for 2 corneodesmosome proteins: desmoglein-1 and desmocollin-1, then observed using confocal microscopy. The distribution of desmoglein-1 and desmocollin-1 across corneocytes was scored from 1 (uniform) to 4 (peripheral). Transepidermal water loss (TEWL), skin-surface-pH, and protease activity were also measured in both cohorts.

**Results:** In AD there was a more uniform desmoglein-1 distribution at the SC surface compared to healthy skin (score of 2.96 compared to 3.45), as well as elevated TEWL (16.25g/m2/h compared to 10.92g/m2/h), skin-surface-pH (4.97 compared to 4.75), and protease activity (tryptic – 2.74nU/µg compared to 0.51 nU/µg, chymotryptic – 1.52nU/µg compared to 0.96nU/µg, and caseinolytic – 7.08nU/µg compared to 2.51nU/µg). There was also a reduction in corneocyte size (718µm2 compared to 828µm2) and SC thickness (4.15µm compared to 5.38µm). In soap-induced xerosis there was a more peripheral desmoglein-1 and desmocollin-1 distribution at the SC surface compared to untreated skin (score of 3.77 compared to 3.39, and a score of 2.57 compared to 1.48, respectively), as well as elevated TEWL (21.35g/m2/h compared to 14.5g/m2/h), skin-surface-pH (7.35 compared to 5.98), and protease activity (chymotryptic – 4.75nU/µg compared to 0.68nU/µg).

**Conclusions:** In AD, the altered surface degradation pattern suggests increased proteolysis of peripheral corneodesmosomes as a result of elevated protease activity, leading to premature SC shedding. The opposite effect is seen in soap-induced xerosis, whereby elevated protease activity appears to accelerate the loss of all but peripheral corneodesmosomes, leading to xerotic skin. In both instances, elevated SC proteases resulted in reduced skin barrier function.