Correlation of 12-LOX activity and hp70 with barrier function
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The evaluation of HP70 is an essential measure in the skin care industry in order to assess the safety and the efficacy of active ingredients. 12-LOX (gene ALOX12B) is a lipoxygenase expressed in keratinocytes and is implicated in the coagulation of the eicosanoid hydroxyicosatetraenoic acides (HETEs) that have a required process to their covalent linkage to proteins of the corneum envelope. It is an important step in establishing the water barrier by preventing unnecessary evaporation through epithelial cells. HP70 family members are among the most abundant HpS in the skin expressed constitutively within keratinocytes. HP70 expression is elevated in both epidermis and dermis for cytoprotection after skin samples are heat shocked or after stressors like UVB. Traditionally, transdermal water product (TEWL) has been widely used as a way to evaluate skin barrier function and tape stripping as a way to evaluate barrier function (biodrometers). Our aim was to understand how HP70 regulates this aspect. 12-LOX and HP70 could be correlated clinically. Subjects were treated with a hydrating cream for 3 weeks on their lower inner forearm. After treatment, TEWL was measured and tape strips were collected from the treatment area and untreated site. 12-LOX enzyme activity was measured with a fluorosence-based assay and HP70 by ELISA using the protein samples isolated from the tape strips. The 12-LOX enzyme activity had a negative correlation with TEWL as previously described and had a positive correlation with HP70. Moreover, HP70 also had a negative correlation with TEWL confirming the correlation between the two biomarkers 12-LOX and HP70 with barrier function. The study of these two biomarkers is a new interesting and non-invasive approach for studying skin under different conditions.

Physiological function of krox20 (fgz2) in epidermal stem cells
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Resident stem cells (SCs) within tissues are important for normal homeostasis maintenance and differentiation. Metabolic analysis of keratinocyte differentiation that detects >10,000 analytes in all major metabolite classes was performed and unexpectedly, glucose was a top increased analyte of the 614 that changed significantly. Functional studies in epidermal tissue showed that intracellular glucose elevation was essential for differentiation. Metabolites in glucose catalytic pathways were unchanged in differentiation, suggesting that the accumulated pool of glucose itself was required. Consistent with this, decreasing cellular glucose levels, by restricting available glucose or by increasing intracellular glucose catalyzing enzymes, HK1/2 and GAPD, blocked differentiation. Knockout and pharmacologic inhibition studies demonstrated that 3 glucose transporters, GLUT1, GLUT1 and SLCT1, were essential for glucose accumulation and differentiation. Furthermore, RNAseq analysis of glucose-depleted epidermal tissue revealed >10% of the expressed genes relevant to the epidermal phenotype on gene signature. ATACseq identified candidate transcription factors (TFs) that may act on glucose-regulated genes, including ZNF750, NFE2L2, and IRF6. Glucose: affinity chromatography followed by mass spectrometry identified the IRFs TF as a glucose binding protein. IRFs was essential for epidermal differentiation and was verified to bind glucose directly at high affinity. Glucose was found to enhance IRFs binding to its cognate DNA binding sequence. Interestingly, an intrinsic epidermal dysplasia and cancer displayed diminished glucose binding. These data support a model in which epidermal differentiation requires upregulation of specific glucose transporters that enable accumulation of free intracellular glucose, which in turn binds to IRFs and enables IRFs DNA binding and IRFs-driven differentiation gene induction.