



ACNE, ROSACEA, AND RELATED DISORDERS (INCLUDING HIDRADENITIS SUPPURATIVA)

REVEALING BARRIER ALTERATIONS IN ROSACEA SKIN AT THE MOLECULAR LEVEL

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Introduction: Rosacea is a common, chronic inflammatory skin disease usually developing in adults. Rosacea mainly affects the sebaceous gland rich (SGR) skin areas, such as cheeks, nose, chin, and forehead. Although clinical data (skin dryness) and previous functional studies (elevated pH and TEWL) of affected skin indicated barrier alterations, the detailed analysis of barrier damage at the molecular level is completely missing in rosacea.

Objective: We aimed to investigate the permeability barrier alterations of rosacea skin by different molecular biology methods.

Materials and Methods: RNASeq has been performed on 8 SGR and 8 rosacea skin samples to reveal gene expressional differences. Pathway analyses were performed by Cytoscape software ClueGo application. Validation of expression levels were performed by RT-PCR and immunohistochemistry.

Results: 5136 gene showed significantly different expression; 3133 genes showed higher, whereas 2003 genes exhibited lower expressions in rosacea samples (fold change $\geq 1,5$). Pathway analysis revealed multiple genes exhibiting roles in the formation of skin barrier and cell junctions in rosacea samples. In our further investigations we focused on validating the expression of these genes. In rosacea, markers having role in proliferation (KRT6, 16, 17) showed significantly higher expression while molecules taking part in differentiation (FLG, LCE1, LOR, KRT1, 10) and cell junction formation (CLDN1, 16, 23, CDH1, CDSN, DSC1, DSG1, PKP1) were significantly downregulated compared to SGR. The expression of antimicrobial peptides (S100A7,8,9, hBD2, LCN2, LL37) was also significantly higher in





rosacea.

Conclusions: Besides the well-known dysregulation of immunological, vascular and neurological functions, we could prove at the molecular level that a prominent barrier alteration is also present in rosacea, which highlights the importance of barrier repair therapies in the present and their further development in the future.

