108 Antimicrobial peptide hBD-3 improves Th2 cytokine-mediated impairment of tight junction barrier through autophagy activation

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109 IL-4 and IL-13 cytokines drive sex steroid hormone synthesis and lipid abnormalities in sebocyte during atopic dermatitis pathogenesis

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One of the hallmark features of atopic dermatitis (AD) is an elevation of the type-2 cytokines, IL-4 and IL-13. Thus, the development of a monoclonal antibody against the IL-4 receptor, Dupilumab, has revolutionized therapy for AD patients. Though the central role of IL-4 and IL-13 in AD is clear, we still have an incomplete understanding of how these immune cyto-
kines drive changes in the skin epithelium. Sebaceous glands are specialized sebum-pro-
ducing epithelial cells that release a mixture of lipids, free fatty acid, and antimicrobial proteins to the skin surface. Little is known about how sebocyte biology changes in AD. Here we show the impact of type-2 cytokines on sebocytes and find that IL-4 and IL-13 stimulate the expression of 3-beta-hydroxysteroid dehydrogenase (3β-HSD1), a rate-limiting enzyme in sex steroid hormone synthesis. Using liquid chromatography-tandem mass spec-
trometry, we demonstrate that IL-4 and IL-13 can enhance HSD1B1 dependent androgen production. Further, in an HSD1B1 dependent manner, IL-4 and IL-13 drive lipid abnor-
malities in human sebocyte cells through regulation of INSIG1 expression. Consistent with our findings in sebocytes, the expression of HSD1B1 is highly elevated in the skin of AD patients and can be restored by Dupilumab treatment. Taken together, these data suggest that targeting sex steroid hormone synthesis pathway could be a potential therapeutic avenue to restore normal skin barrier function in AD patients.

110 Deletion of TNAFIP6 gene in human keratinocytes by CRISPR/Cas9 edition demonstrates a role for TSG-6 to retain hyaluronan inside epidermis

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We previously showed that TSG-6, an immune modulatory enzyme in sex steroid hormone synthesis. Using liquid chromatography-tandem mass spectrometry, we demonstrate that IL-4 and IL-13 can enhance HSD1B1 dependent androgen production. Further, in an HSD1B1 dependent manner, IL-4 and IL-13 drive lipid abnormalities in human sebocyte cells through regulation of INSIG1 expression. Consistent with our findings in sebocytes, the expression of HSD1B1 is highly elevated in the skin of AD patients and can be restored by Dupilumab treatment. Taken together, these data suggest that targeting sex steroid hormone synthesis pathway could be a potential therapeutic avenue to restore normal skin barrier function in AD patients.